

PHARMACOLOGY AND
EXPERIMENTAL THERAPEUTICS



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AND EXPERIMENTAL
THERAPEUTICS

A Survey for 1941-1946

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INTRODUCTION

DURING the war years many new medicinal agents were introduced and many drugs were restudied in various species. This period was characterized by greatly increased activity in research laboratories and clinics throughout the free world. Many studies related to the war effort have been published only recently. Despite the feverish tempo and attempts at coordination of the work of various laboratories on combined projects, there is no single reference in which these studies are summarized.

The present survey is an attempt to bring together significant studies in the field of applied pharmacology and toxicology. Quantitative data only are included, in an effort to relate dosage to specific effect. Whenever blood or other tissue levels of an effective agent are reported, these are listed. Each medicinal agent is recorded under its accepted name, and whenever synonyms or chemical names are known, they are given.

In vitro effects and *in vivo* activities in the several species and especially in man are summarized. Beneficial as well as harmful effects produced by known amounts of biologics or chemicals are recorded briefly. Biologic tests used to identify agents, and chemical techniques utilized for detecting important drugs or poisons in body fluids or tissues, are listed also.

Since no effort has been made in recent years to record poisoning resulting from exposures to new industrial or agricultural agents, or even to medicinals, references in this area are included. Actually, the only German publication which covered the field of toxicology has been discontinued, and no current reference is now available. In the present survey not only are toxic dose levels for animals dealt with after the manner of Sollmann and Hanzlik, *Fundamentals of Experimental Pharmacology* (J. W. Stacey, Inc., San Francisco, 1940), but data on man are stressed particularly. No effort has been made to duplicate material covered by Sollmann and Hanzlik, or to review any other source than the current medical and toxicologic literature.

Under each agent included in the survey, there is first noted the species, or, if that terminology is not applied, then the technic for identification or other test or characteristic, second, the effect produced, third, the dose

level (in mgm. per kilo whenever given); fourth, other data on the effects produced, whether beneficial or harmful; fifth, the author, reference source, volume of journal, page, and year of publication.

A conscientious effort has been made to cover not only medical literature, but also the literature of experimental biology, veterinary medicine, dentistry, pharmacy, and related special fields as well. No survey of this sort could hope to be entirely complete, but, with one or two exceptions, most of the agents of current interest are covered. The exceptions are the antibiotics, notably penicillin and streptomycin, the antimalarials, and the sulfonamides. Annotated bibliographies which serve as satisfactory reference sources for these may be found elsewhere. To include such material again would double the size of the present volume and duplicate what is readily available. Only a few of the more pertinent articles on these subjects are included in the present survey. Other sources are listed.

Since this is purposely a critical survey of accepted publications, many articles have not been included. For example, nondescript, trade-named preparations of a proprietary nature are not reviewed. Nor will one find reference to articles which have appeared in journals which publish material not acceptable generally in the scientific press. Annual reviews, monographs, and books which contain data relating to drugs are not included. In effect, duplication has been avoided whenever possible.

The present survey is designed merely to record the progress of basic research and clinical investigation during the war years. To put the aggregate of our advances in one place for ready reference may be of advantage to many basic research, clinical, and commercial laboratories. Not only in the United States, but particularly abroad, a record of this kind may prove useful. It is hoped that this survey —

must have a suggestion of the parts which will make the whole picture clearly visible.

It is hoped that workers in basic-science laboratories, and graduate students, as well as professional personnel, may find the survey of some help and interest in the postwar years ahead.

THE COMPILERS.

A Survey of

PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS

ACACIA

Dogs--

Intravenous Effect: Intravenously sufficient 6% acacia in 0.06% sodium chloride given for 76 days to maintain serum levels of 1.5-3.5% produced one death in three animals four months after the last injection. Enlarged liver with large amounts of stored acacia was seen at autopsy. Acacia remained in the blood of surviving animals up to 26 months. Livers were enlarged from a quarter to twice normal size and became lighter in color. Smalley, et al., Arch. Int. Med., 76: 39 (July) 1945.

Experimental Hemorrhage: 6% solution in 0.85% sodium chloride was effective in acute hemorrhage. Liver cells contained acacia but were not damaged by it. Sloan, Block and Frejlich, Anesth. & Analg., 21: 343 (Nov.-Dec.) 1942.

Man--

Nephrotic Edema. Intravenously 90-325 gm. in 8 to 56 days plus mercurophylline, given subsequently in six patients effected gradual elimination of nephrotic edema. Johnson and Newman, Arch. Int. Med., 76: 167 (Sept.) 1945.

Treatment of Nephrosis: Total dose of 330 gm. was given in 11 infusions of 500 ml. of a 6% solution of acacia in a 0.06% of sodium chloride. Lehnhoff and Binger, Proc. Staff Meet. Mayo Clin. 17: 30 (Jan.) 1942

ACETALDEHYDE

Rats--

Toxicity Intraperitoneal 50 mgm/100 gm. Killed within 10 minutes.
Metabolism. 20 mgm. rapidly metabolized, so that a total of 250 mgm may be given at 15 minute intervals. Stotz, Westerfeld and Berg, J. Biol. Chem., 152: 41 (Jan.) 1944.

ACETANILIDE

Animals (various)—
Acute Toxicity:

Frogs—Heart perfusion: L.D., 3,500 parts per million;
Mice—Oral: T.D., 1,840 mgm/kg.;
Subcutaneous (in 55% alcohol): T.D., 1,200–1,350 mgm/kg.,

L.D., 1,200–1,350 mgm/kg.;
Rats—Oral: LD₅₀ (in acacia), 400 mgm/kg.,
LD₅₀ (in acacia), 800 mgm/kg.,
LD₁₀₀ (in acacia), 1,200 mgm/kg.,
LD₁₀₀ (in 50% alcohol), 2,400 mgm/kg.;

Guinea Pigs—Oral: L.D., 1,400–1,500 mgm/kg.;
Rabbits—Oral: T.D., 1,200 mgm/kg., L.D., 1,500 mgm/kg.;

Cats—Oral: L.D., 250 mgm/kg.,
Intravenous: L.D., 8.0–13.5 mgm/kg.;

Dogs—Oral: T.D., 750–1,000 mgm/kg.; L.D., 700–1,000 mgm/kg.;

Intravenous: T.D., 62.5–75.0 mgm/kg.; L.D., 175–300 mgm/kg.;

Monkeys—Oral: T.D., 600 mgm/kg.; L.D., 300 mgm/kg.;

Intravenous: T.D., 275 mgm/kg.; L.D., 5–250 mgm/kg.;

Man—Oral: T.D., 25–500 mgm/kg.; L.D., 5–250 mgm/kg.;

Munch, Pratt, and Phillips, J. Am. Pharm. A., 30: 91 (Apr.), 1941.

Pain Threshold: Increase was 4.3% in eight patients given 0.015 gm. acetanilide, 0.06 gm. caffeine and 0.3 gm. sodium bromide in effervescent base. Actual effectiveness of mixture alone equaled 6.4% rise in pain threshold. Ledus and Slaughter, Anesth. & Analg., 24: 147, 1945.

ACETARSONE

(N-acetyl-4-hydroxy-m-arsanilic acid)

Man—

Congenital Syphilis (children): Oral 0.005 gm/kg. for 14 days, 0.01 gm/kg. for 14 days, 0.015 gm/kg. for 14 days, and 0.02 gm/kg. for 28 days. Dosage for central nervous system or syphilitic keratitis should be increased $\frac{1}{4}$ – $\frac{1}{2}$ more. At end of ten weeks intramuscular bismuth sub-salicylate one time weekly $\frac{1}{8}$ –1.5 ml. depending on age and size of child. Killingsworth, Texas State J. Med., 38: 17 (May) 1942.

Pemphigus Erythematodes: 0.25 gm. tablets (200–400) plus other therapy. Zakon, Arch. Dermat. & Syph., 45: 791 (Apr.) 1942.

Experimental Therapeutics

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Trichomonas Vaginalis Therapy: Insertion of medicated tampons containing 0.03 gm. acetasone dusted with 0.1 gm. acetasone. Feresten, M. Record, 155: 130 (Feb.) 1942. Tampons containing 0.1 gm. plus dusting. Meigs, New England J. Med., 226: 562 (Apr.) 1942.

Vincent's Infection: Oral 0.25 gm. two times daily for seven days is effective when local treatment proved inadequate. Erskine, Brit. M. J., II: 729 (Dec.) 1943.

ACETIC ACID

Man—

Pseudomonas pyocyanea infection: 2% acetic acid was recommended at Australian Gen. Hosp., Rank, Australian & New Zealand J. Surg., 11: 171 (Jan.) 1942.

Douches: 20–75 ml. red or white vinegar in 1000 ml. tap water. Buffered solution of pH 4.5–5.0 or unbuffered solution of pH 2.9 was best for vaginal douches. Normal vaginal pH was 3.9–5.0 (average 4.2). Karnaky, Am. J. Surg., 69: 107 (July) 1945.

ACETONE

Man—

Toxicity. 50 mgm/L. was maximum industrial concentration, although blood levels of 330 mgm/L. may develop even at this concentration. Haggard, Greenberg, and Turner, J. Ind. Hyg. & Toxicol., 26: 133 (May) 1944.

ACETOPHENETIDIN

Man—

Sulfhemoglobinemia. Orally, 0.5–1.3 gm. was given two years to one patient and in another 16 gm plus 8 gm. of acetanilide were taken in two weeks. Lazarus, Brit. M. J. II 565 (Oct.) 1945.

P-ACETYLAMINO HIPURIC ACID

Mice (white)—

LD₅₀: Intravenous dose, 5.25 + 0.5 gm/kg. Mattis et al., J. Pharmacol. & Exper. Therap., 84: 147 (June) 1945.

ACETYLCHOLINE

Rats—

Potentiation. By alcohol and ether on both normal and eserized frog's rectus abdominis. Increased with increased concentration up to

A Survey of Pharmacology and J. Pharmacol. & Exper. Therap., 73: 119 (Oct.) 1911.

Acuolation of Pancreas Acinic Cells: Produced with 1 mgm. hourly times three, diminished effect of previously thyroidectomized. Increased effect if 0.3 mgm. thyroxin were given daily over previous several days. Leblond, Seigeyeva, Anat. Rec., 90: 235 (Nov.) 1914.

Man—

Paroxysmal Tachycardia: Intravenously, 0.01–0.1 gm. in 5% solution arrested in 30 seconds (65 attacks). Segers and Denolin, J.A.M.A., 129: 226 (Sept.) 1915.

Treatment of Schizophrenia: Intravenous therapy (slight margin of safety). Cohen, Thale and Tissenbaum, Arch. Neurol. & Psychiat., 51: 171 (Feb.) 1914.

Mice, Rats—

ACTINOMYCIN

Acute Toxicity: 1 mgm/kg. single dose oral, subcutaneous, intravenous, or intraperitoneal killed the animals. 50 γ/kg. for 6 days killed. Robinson and Waksman, J. Pharmacol. & Exper. Therap., 74: 25; 1912.

Chronic Toxicity: Liver and kidney functions impaired; spleen showed shrinkage. Ibid.

Rabbits—

2.5 γ/20 gm. intravenously was followed by excretion of 10–20% in urine in six hours. Ibid.

Rats—

ADENINE SULFATE

Diuretic Action: 137 times that of urea. Lipschitz and Stokely, J. Pharmacol. & Exper. Therap., 83: 235 (Apr.) 1915.

Tolerated Dose: 1.55 mM/kg. Ibid.

Diuretic (useful) Dose: 0.062–0.217 mM/kg. orally. Ibid.

Dogs—

Diuretic Action: 72.5 times that of urea. Diuresis was maximum in 1–3 hours. Ibid.

Man—

ADENYLIC ACID

Pellagra: Intravenous 50 mgm. daily for two to five days cleared mouth ulcers. Vilter, Bean and Spies, J. Lab. & Clin. Med., 27: 527, 1912.

Rapid Injection: 5–10 mgm. in 20 seconds caused flushing, deep inspiration, transient tachycardia, sensation of suffocation and impending disaster. *Ibid.*

Slow Injection: 2.0 mgm./minute produced mild hyperpnea, tachycardia, abdominal cramps, tingling in mouth and mild apprehension. *Ibid.*

ADRENAL CORTEX EXTRACT

Man—

Perennial Vasomotor Rhinitis: Injection of 0.5 ml. with 0.1 ml. of a 1:10,000 dilution of epinephrine twice daily diminished odor in the nasal mucosa and the amount of watery secretion in 14 of 15. Williams, *Proc. Staff Meet., Mayo Clin.*, 20: 273 (Oct.) 1945.

β -ALANINE

Man—

Organ Content: Found only in liver (150r) and pancreas (7.5r)/gm. dry substance. Nielsen, Hartelius and Schmidt, *Naturwissenschaften*, 31: 550 (Nov.) 1943.

ALBUMIN

Rabbits—

Urinalysis: Massive doses of penicillin caused highly positive albumin reaction. 25% by volume acetone or ethyl alcohol added to 5 ml. of urine prevented pseudo albumin reaction, if <10–13 mgm. penicillin was present. Perlstein, et al., *Yale J. Biol. & Med.*, 18: 11 (Oct.) 1945.

Man—

Liver Function Tests. A fall below 2 gm. albumin/100 ml. plasma was a grave prognostic sign of permanent liver damage. Higgins et al., *Brit. M. J.*, 1: 211 (Feb.) 1944.

ALCOHOLS, AMYL

Rats—

Blood Concentration: Four intraperitoneal injections of 1.0 gm./kg. of seven amyl alcohol isomers at 15 minute intervals were given. 11–55 mgm.% primary alcohol was the blood concentration at one hour; the alcohol disappeared from the blood in 3.5–9 hours, 51–65 mgm.% secondary alcohol in 13–16 hours, and 123 mgm.% tertiary alcohol in over 50 hours, respectively. Haggard, Miller and Greenberg, *J. Indust. Hyg & Toxicol.*, 27: 1 (Jan.) 1945.

Fate: 1.2-7.6% of primary alcohol was eliminated, the rest was metabolized to aldehydes and acids. >90% secondary amyl alcohol not eliminated was converted to ketone. 35% of tertiary alcohol appeared in expired air and urine, 65% was metabolized. *Ibid.*

Toxicity: Basic lethal amount was 0.61 gm/kg. for pentanol-1, 1.2-methyl butanol-1, and 3-methyl butanol-1; 8.8 gm/kg. for 2-methyl butanol-1; 1.53 gm/kg. for 2-methyl butanol-2; 1.25, 1.25 and 1.02 gm/kg. for methyl-n-propyl ketone, diethyl ketone, and methyl-isopropyl ketone, respectively. *Ibid.*

ALCOHOL, BUTYL (BUTANOL)

Man—

Asthma: 50% larger doses as effective as epinephrine without by-effects. Tainter, et al., quoted by Suter & Ruddy, J. Am. Chem. Soc., 66: 747 (May) 1944.

Circulation: Improved by lowering diastolic blood pressure and increasing pulse rate without proportionately raising cardiac work. *Ibid.*

Tolerance: 1/100 as toxic as epinephrine. *Ibid.*

Toxic Effects: Exposure to concentrations of 15-100 p.p.m. produced ocular irritation, dermatitis, headache, vertigo, upper respiratory tract irritation. Tabershaw et al., J. Indust. Hyg. & Toxicol., 26: 328 (Dec.) 1944.

ALCOHOL, ETHYL

Dogs—

Metabolic Rate of intravenous ethyl alcohol was not altered by (a) two subcutaneous injections of insulin 1 U/kg. three hours apart, (b) oral 3 gm. glucose, (c) insulin and glucose. Alcohol disappeared from the blood in 11 hours. Gregory, Ewing and Duff-White, Proc. Soc. Exper. Biol. & Med., 54: 206 (Nov.) 1943.

Intravenous or oral 0.5 gm. sodium pyruvate/kg. in 5% solution did not alter ethyl alcohol metabolism. *Ibid.*, 54: 209 (Nov.) 1943.

Man—
Alcohol Poisoning Therapy: Intravenous administration was effective in treatment of alcoholic patient with delirium and hallucinosis or with craving. Solution is prepared by mixing 33 ml. 95% alcohol quantity sufficient 30% glucose to make 100 ml. This was divided into 5 ampules of 20 ml. each. Dose 60-80 ml. first day, gradually less for the next six to seven days. Carrotala, Semana Méd. (Buenos Aires) 48: 1274, 1941, through Digest of Treatment, 6. 62 (July) 1942.

Higher Nervous Activity: 1.5-2 ml/kg. body weight caused marked decrease in perception of electric shock and feeling of pain under faradic stimulation. Interfered with negative conditioned responses and tended to convert inhibitory response to excitatory reaction. Respiratory conditioned reflex temporarily impaired and respiratory rate slowed down markedly. Finklestein, Alpern and Gantt, Bull. Johns Hopkins Hosp., 76: 61 (Feb.) 1915. (See Benzedrine Sulfate.)

Lower-half Headache with symptoms referable to sphenopalatine ganglion—cocainization aborts attack; injection of 95% alcohol and 5% phenol into ganglion increased pain temporarily and then relieved for six months to three years. Girling, Northwest Med., 41: 418 (Dec.) 1912.

Popliteal Nerve Injury: Paravertebral injection of procaine, and also injection of 3-4 ml. 80% alcohol, brought complete relief in three patients and partial relief for three months in two patients. Hirshmann, Nervenarzt, 16: 25 (Jan.) 1913; Bull. War Med., 4: 139 (Nov.) 1913.

For *diffuse peritonitis and paralytic ileus*, vomiting, low fluid or caloric intake: Intravenously, from 30-60 ml, U.S.P. 95% in 1,000 ml. 5% glucose in normal saline or distilled water were administered. Stone and Cleveland, Clinics Virginia Mason Hosp., (Seattle, Washington) 20: 58 (Dec.) 1911.

Alcoholic Psychosis. Intravenous therapy with 5% saline. Patients with decompensated cardiac disease were given 1.5 or 2.5% saline subcutaneously. Silverman, M. Ann. District of Columbia, 13: 102 (Mar.) 1914.

Anesthesia: 500-800 ml. intravenously of 25%_o. Duration 1-1½ hours. Gorelov, Voennno sanit. delo., #8-9: 47, 1913.

Sedative. Intravenously, 50 ml. pure 95% ethyl alcohol added to 1,000 ml. 5% glucose in saline, injected at rate of 60 drops per minute. Behan, Am. J. Surg., 69: 227 (Aug.) 1915.

Sepsis Inhibited. 500-800 ml. intravenously of 25%_o, duration one to one and a half hours. Gorelov, Voennno sanit. delo., #8-9: 47, 1913.

ALCOHOL, ISOPROPYL

Cold Sterilization: 40% killed *Staphylococcus aureus* in five minutes at 20°C., 30% killed *E. coli* in five minutes. Powell, J. Indiana M. A., 38: 303 (Sept.) 1915.

Sterilization: One liter isopropyl alcohol, 2 ml. oil of rose geranium, 4 ml. oil of cinnamon or cassia, 780 ml. distilled water, 4 gm. sodium

nitrate, 60 ml. monoethanolamine or triethanolamine, and 160 ml. solution of formaldehyde U.S.P. mixed in order given killed pyogenic organisms readily and in 15 minutes insured complete absence of bacteria. Most resistant spores killed in five hours. Tainter et al., J. Am. Dent. A., 31: 479 (Apr.) 1944.

Sterilization of Metal Instruments: 100% was stronger germicide against vegetative forms than 70% and less corrosive. J.A.M.A., 119: 1387 (Aug.) 1912.

Various Species—

Acute Toxicity: Approximately twice as lethal as ethyl alcohol, and salivation, retching, and vomiting appeared more often. Sequence of terminal symptoms were same for both. Lehman and Chase, J. Lab. & Clin. Med., 29: 561 (June) 1914.

Rats—

Chronic Toxicity: Repeated doses of 0.75–5.28 ml/kg. either augmented or very slightly decreased growth without delayed effects. Ibid.

Guinea Pigs—

Toxicity: Oral, 10% isopropanol, totaling 1 ml. pure isopropyl alcohol daily for 20 days produced no toxic manifestations and animals appeared normal at autopsy. Harris, J. Am. Pharm. A., Pract. Pharm. Ed., 5: 38 (Feb.) 1914.

Dogs—

Intradermal Injection. <0.1 ml. in dog's abdomen produced an area of necrosis which eventually sloughed, leaving sluggish ulcer. *Intra-arterial Injection:* 0.5 ml. caused perceptible hemolysis in circulating blood but no other toxic effects with 2 ml. J.A.M.A., 128: 986 (July) 1945.

Cattle—

Toxicity: 15–30 ml. doses containing 20% isopropanol were non-toxic. Harris, J. Am. Pharm. A., Pract. Pharm. Ed., 5: 38 (Feb.) 1914.

Horses and Cows—

Chronic Toxicity: Oral, several hundred doses of 60 ml. containing 12.5% isopropanol were non-toxic. Ibid.

Man—

External Application. 50 and 100% isopropanol three times daily to approximately 300 sq. cm. of arms of three persons for 25 days gave no evidence of skin irritation or absorption. Ibid.

Man—

ALCOHOL, METHYL

Therapy of Poisoning: By repeated drinking of ethyl alcohol, oxidation of methyl alcohol to formic acid was checked. Intravenous 1.3% sodium bicarbonate was administered, and fluid intake was increased. Eyes were protected from strong light, and metabolic stimulants were avoided. *Roe, Acta med. Scandinav.*, 113: 558, 1943.

Toxicity: LD was 120–140 gm., but blindness resulted in some cases after 8–20 gm. The drug was present in blood even days after ingestion, therefore fatal dose was reached by cumulation. Toxic symptoms were: violent headaches, vertigo, painful colic, mydriasis, amaurosis, paralysis of legs, dyspnea, loss of consciousness, death from respiratory paralysis. Potassium bicarbonate or sodium bicarbonate produced partial detoxification. *Chambou, Lyon pharm.* (June) 1943, through *Schweiz. Apoth. Ztg.*, 81: 924 (Dec.) 1943.

Dogs—

ALCOHOL, POLYVINYL

Effect: Intravenous 1 gm/kg. of 5% solution in physiologic saline. Marked tubular degeneration, damage to glomerular tufts, endothelial swelling filled with alcohol. Tubular lumina and epithelial lining also contained alcohol, also liver and spleen tissues, indicating animal is unable to break up and eliminate compound. Marked decrease in all blood values, especially white blood cells. Sedimentation rate very rapid, one-half hour after injection and did not reach normal 45 days later. All lost appetite and weight. *Young, Mulay and Chrisue, J. Lab. & Clin. Med.*, 27: 1131 (June) 1942.

ALDARSONE

(4-hydroxy-N-sulfomethyl-m-arsanilic acid)

Man—

Central Nervous System Syphilis: 1 gm. dissolved in 10 ml. sterile distilled water, intravenously, once weekly, for 40 to 50 weeks. *A.M.A., Council on Pharmacy and Chemistry, J A M A.*, 123: 969 (Dec.) 1943.

Neurosyphilis. 25 patients were treated by three hours of artificial fever, 105°F., every three to seven days for 16 to 17 heatings, 0.01 gm. bismuth salicylate intramuscularly before each heating and 0.25 gm. aldarson intravenously at the height of fever in the first heating, 0.5

gm. in the second, and 1.0 gm. thereafter. Full clinical remission in 8 patients with paresis and one with meningovascular neurosyphilis, partial improvement in 8 with paresis and no improvement in 5 with paresis, 2 with juvenile paresis and 1 with taboparesis. Bennett, Morrison and Modlin, Ven. Dis. Inform., 25: 69 (Mar.) 1944.

ALIPHATIC AMINES

2-methyl-amino-heptane (Amethine)

Frogs—

Heart Rate Decreased: 1% concentration causes complete stoppage with 2%. Jackson, J. Lab. Clin. Med., 29: 150 (Feb.) 1944.

Heart Rate Increased: 0.05% concentration. Ahlquist, J. Pharmacol. & Exper. Therap., 81: 235 (July) 1944.

Heart Rate Decreased: 1% concentration, inhibition complete with 2% concentration (HCl). Ibid.

Rats—

LD₅₀: 42 mgm/kg. (sulfate). Ibid.

LD₅₀: 64 mgm/kg. (bitartrate). Ibid.

LD₅₀: 47 mgm/kg. (HCl). Ibid.

Dogs—

Depressor Response: Definite with 2 mgm/kg. Average duration 40 minutes. Ibid.

Pressor Response: With 2 mgm/kg. slight. Ibid.

Maximum Pressor Response: 2 mgm/kg. Average duration 40 minutes. Ibid.

Blood Pressure Rise: Prompt, more persistent and stable than with epinephrine. Ibid.

Central Nervous System: Therapeutic amounts exhibit little direct effect. Ibid.

Pressor Effect: Moderate with 2 mgm/kg. Average duration 40 minutes. Ahlquist, J. Pharmacol. & Exper. Therap., 81: 235 (July) 1944.

Shock: 0.25 ml. 10% solution intravenously HCl (therapeutic) approximates effect of 0.25 ml. 1:1,000 epinephrine HCl. Jackson, J. Lab. & Clin. Med., 29: 150 (Feb.) 1944.

Toxicity. Orally, relatively low. Ibid.

ALIZARINE RED S

(Sodium alizarinsulfonate)

Measurement of Growth by Vital Staining: 2% in 0.15% sodium chloride intraperitoneally produced red line in bone and dentin calcifying at the time.

Rat, Rabbit, Guinea Pig, Cat, Dog, Monkey, Man (Infant)—

E.D. 50-100 mgm/kg.

Dogs—

10 ml, 2% intravenously, no change in respiration or blood pressure. Intraperitoneally, most effective, least toxic. Schour, Hoffman, Sarnat. *Engel, J. Dental Research*, 20: 411 (Oct.) 1941.

ALLOXAN

Mechanism of Action. Intravenously, 1 unit insulin per kg. simultaneously with 150-200 mgm alloxan per kg. prevents initial alloxan hyperglycemia, but does not prevent destruction of islet cells or diabetes development. Alloxan seems to act by damaging the beta cells directly rather than as insulin inhibitor. Goldner and Gomari, *Proc. Soc. Exper. Biol. & Med.*, 55: 73 (Jan.) 1944.

Rats—

Action. Subcutaneously 300 mgm alloxan per kg. caused histologic changes within five minutes in pancreatic tissue but evidence of hyperplastic reaction or stimulation of insulin-produced mechanism was not observed. Hughes, Ware, and Young, *Lancet*, 216: 148 (Jan.) 1941.

350 mgm/kg body weight in 4 equal doses per 15 minutes showed progressive destruction of islet cells of pancreas up to seven hours and reduction of pancreatic insulin. At 18 hours islet structure seemed restored but insulin content reduced. Ridout, Ham and Wienshall, *Science*, 100: 57, 1941.

Diabetes Mellitus produced by single intraperitoneal injection 200 mgm/kg. Necrosis and complete disappearance of beta cells from pancreatic islets. Gomori and Goldner, *Proc. Soc. Exper. Biol. & Med.*, 51: 287 (Dec) 1943.

Rabbits—

Diabetes. Intravenously 200 mgm/kg caused rapid death due to damage of beta cells of the islets of Langerhans. Duffy, *J. Path. & Bact.*, 57: 199 (Apr) 1945.

Cats—

Diabetic Action: Oral 0.5–1 gm/kg. (higher for immature than mature) in food taken at once. 6–12 hours later milk given and next day their usual diet of milk and raw meat. Ruben and Yardumian, Science, 103: 220, 1946.

Dogs—

Injurious Action: Intravenous 200–500 mgm/kg. fatal in one hour to six days. Death associated with significant increase in blood glucose and blood protein N. Necrosis of islet cells in pancreas and epithelium of convoluted tubules of kidney. Brunschwig et al., J.A.M.A., 124: 212, 1944.

150 mgm. in 4 doses showed decrease in insulin per gm. of total pancreas after islet cells were necrotic. The same dose to depancreatized dogs showed no blood sugar reduction. Ridout, Ham and Wrenshall, Science, 100: 57, 1944.

Glycemia: Intravenously 100 mgm/kg. produced glycemia of a degree equal to that following adrenalectomy or section of splanchnic nerve. Insulin secretion stops after 24 hours in 5 of 6. Houssay, Argentine Soc. Biol. Meet., J.A.M.A., 129: 145, 1945.

Man—

Action on Pancreatic Islets: 0.67–1 gm/kg. intravenously over three to four days brought freedom from hypoglycemic shock to patient with islet cell tumor. Blood sugar level as high as 298 mgm. per cent for ten to 21 days. 400 mgm. and 500 mgm/kg. respectively to two patients produced no disturbances. 600 mgm/kg. produced hypoglycemia without primary hyperglycemia within five hours of injection to patient with carcinomatosis. Degenerative changes in islets and hepatic cells. Brunschwig and Allen, Cancer Research, 4: 45 (Jan.) 1944.

ALUMINUM

Man—

Silicosis Therapy: Daily inhalation, at first for five minutes, increased gradually to 30 minutes per day. 55% clinical improvement. Crombie, Blaidell and MacPherson, Canad. M. A., 50: 318 (Apr.) 1944.

Prophylactic Procedure for Silicotic Workers: 60 to 100 treatments at 3 week intervals in above manner. Ibid.

Silicosis Therapy: Inhalation hydrated alumina for five minutes followed by daily five minute increment to 30 minutes effected subjective improvement in 11 of 24. Bamberger, Indust. Med., 14: 477 (June) 1945.

ALUMINUM ACETATE

Man—

Osteitis deformans. Orally, 2.5% solution in elixir controlled Paget's disease within four months in a woman patient. Fazen, Wisconsin M. J., 44: 983 (Oct.) 1945.

ALUMINUM HYDROXIDE

Man—

Peptic Ulcer. >8 ml. $\text{Al}(\text{OH})_3$ gel every two hours during waking hours with 2 hourly feedings for 1 month; 30 ml. at bedtime, repeated at midnight and 3 A.M. for one week for severe night pains. Ambulatory patients six times daily, one hour after meals and interval feedings and at bedtime Collins, J.A.M.A., 127: 899; 1945.

ALUMINUM SULFATE

Removal of Amebic Cysts from Water. Added 0.4–0.66 gm. aluminum sulfate per gallon, allowed to settle one hour, filtered at six gallons per square foot of filtered surface per minute, chlorinated to provide residual of at least one p p m. Bull. U.S. Army M. Dept., 71: 6 (Dec.) 1943.

AMETHOCAINE HYDROCHLORIDE

Mice—

Toxicity: LD_{50} —17.1 mgm/kg. intravenously, LD_{50} cocaine—35 mgm/kg, LD_{50} procaine—87.5 mgm/kg. This was less than reported by Fussanger and Schauman, Bacharach and Middleton, Quart. J. Pharm. & Pharmacol., 14: 356, 1941.

AMETHONE

(AP-46)

(3-(β diethylaminoethyl)-3-phenyl-2(3) benzofuranone)

Man—

Antispasmodic. Intramuscular injection of 100 mgm. every three hours for renal calculi. Intramuscular injection of 100 mgm. for renal and urethral colic. Oral dose of 100 mgm. every three hours for bladder spasm. In cystoscopy use 100 mgm. intramuscularly 20 minutes before instrumentation or 100–150 mgm. orally 30 minutes before. Prince and Richardson, J. Urol., 54: 75 (July) 1945.

Cumulative Effects. None in patient who received 9,600 mgm. in two weeks. *Speed of Action*. 15 to 30 minutes after injection pain subsided.

Toxic Reactions: Stinging at site of injection, dizziness, dry mouth, blurring of vision occurred. Reactions independent of age or physical condition of patient. Ibid.

AMINO ACETIC ACID

Rabbits—

Metrazol Convulsion prevented with glycine 220–880 mgm/kg. five minutes before administration of metrazol. Pollock, Finkelman, Tigay, Proc. Soc. Exper. Biol. & Med., 49: 159, 1942.

Man—

Work Capacity: 4.5–6.0 gm. daily for three weeks did not increase work capacity. King et al., J.A.M.A., 118: 594, 1942.

AMINO ACIDS

Assay—

Microbiologic Method: 1.5 gm. of the sample permitted determination of all essential amino acids, the same basal medium is used for all determinations. Stokes et al., J. Biol. Chem., 160: 35 (Sept.) 1945.

AMINOACRIDINES

(2-chloro-5-(β -diethylaminobutyl)-7-methoxy aminoacridine)

Man—

Tertian Malaria: 30 mgm. three times daily for five days caused fever to subside and parasites to disappear within three days in 27 patients. Bose, Ghosh, and Rakshit, Indian M. Gaz., 79: 601 (Dec.), 1944; through Trop. Dis. Bull., 42: 444 (June), 1945.

AMINO ANTIPYRINES

(4-mono-alkylated)

Solubilization: Water solubility of therapeutic agents increased in presence of these antipyrines, e.g., 0.14 gm. caffeine dissolved in 10 ml. water in presence of 0.9 gm. methyl compound or 1.5 gm. isopropyl compound Skita et al., Ber. d. deutsch. chem. Gesellsch., 75B: 1696, 1942, #12.

Analgesic Activity: Increased with increase in molecular weight of introduced alkyl groups. Ibid.

p-AMINO BENZENE-SULFONYL-THIOUREA

Man—

Excretion: Intrapleurally 20–40 ml. of a 33% solution. Urinary elimination began one hour after administration; reached a maximum in four

to eight hours, and ceased by the second day. In others, began within four hours; reached a maximum in six to 18 hours, and ceased by the tenth day, depending on whether the lungs were healthy or tuberculous Pichat and Gouttebarg, *Compt. rend. Soc. de biol.*, 139, 122 (Jan.) 1945.

Mycobacteria: Intrapleurally 30-40 ml. of a 33% solution daily and then every two days to two tuberculous patients effected disappearance of organisms in three and six weeks respectively. Pichat, *Ibid.*, 139: 124 (Jan.) 1945.

P-AMINO BENZOIC ACID

Member of vitamin B complex. Prevents graying of hair of black and piebald rats.

Chicks—curative dose 300 γ /gm. ration.

Rats—curative dose 3 mgm. daily

Ansbacher, *Science*, 93: 164 (1941)

Toxicity: Mice MLD 2.85 gm/kg, rats >6.0 gm/kg, dogs 1-3 gm/kg. Repeated doses of 0.6-1.4 gm/kg daily for 28 days to rats (stomach tube) —no effect. Scott and Robbins, *Proc. Soc. Exper. Biol. & Med.*, 49: 184, 1942.

Chicks—

Growth: 500 micrograms/100 gm control diet stimulated growth. Briggs et al., *Proc. Soc. Exper. Biol. & Med.*, 55: 130 (Feb.) 1944

Rickettsiae. 2 mgm. inhibited growth of typhus rickettsiae in the yolk sac of the developing egg Hamilton, *Proc. Soc. Exper. Biol. & Med.*, 59: 220 (June) 1945.

Mice—

Action on *Treponema Pallidum*. Subcutaneously, a mixture of 100 mgm. with a suspension of treponema had no pathogenic action; 0.002 gm. did not suppress pathogenicity. Levaditi and Pérault, *Compt. rend. Soc. de biol.*, 139, 7 (Jan.) 1945.

Arsenic Detoxication: Intraperitoneally 500-1200 mgm/kg. or orally 1000-2500 mgm/kg protected mice against LD₅₀ neoarsphenamine (240-280 mgm/kg. intravenously) but not against inorganic arsenious acid, mapharsen, arsphenamine, or tartar emetic. Sandground and Hamilton, *J. Lab & Clin Med.*, 28, 1821 (Dec.) 1943.

Rats—

Thyroid Effect: 3.0% in food for 19 to 45 days caused marked thyroid hyperplasia, basophilia and appearance of "thyroidectomy" cells in the anterior hypophysis, and increased resistance of the animals to lowered

barometric pressures (190 mm. Hg). The drug reduced basal metabolic rate to the same extent as 0.2% thiouracil. Gordon, Goldsmith, and Charipper, *Endocrinology*, 37: 223 (Oct.) 1915.

Toxicity: Intravenously 4 gm/kg. killed 30%, convulsions and respiratory paralysis; intraperitoneally 4 gm/kg. 40% died. Orally, no death unless 6 gm/kg. fed for three successive days. Richards, *Fed. Proc.*, II: 71; 1942.

Guinea Pigs—

Spotted Fever: 2% in high protein fed to 12 guinea pigs; started 24 hours before infection with Rocky Mountain spotted fever and continued through incubation period, reduced mortality rate from 100% to 16.6%; seven remained afebrile. 60% of those treated on day of infection and 30% of guinea pigs treated 72 hours after infection remained afebrile. Anigstein and Bader, *Science*, 101: 591 (June) 1915.

Rabbits—

LD₅₀ intravenously, 2 gm/kg. Ibid.

Man—

Toxic Reaction from 4 gm. oral before and 1–2 gm. after administration of arsenical were not inhibited. Rose et al., *Am. J. Syph. Gonorr. & Ven. Dis.*, 28: 103 (Jan.) 1944.

Thyrototoxicosis: 1.0 or 1.5 gm. sodium salt given six times a week, was effective in treatment of six patients. Basal metabolic rate and pulse rate reduced to normal, serum cholesterol increased and weight gain was resumed. Berman, *Proc. Soc. Exper. Biol. & Med.*, 59: 70 (May) 1945.

2-AMINO-HEPTANE SULFATE

Man—

Nasal Constrictor: 0.5% and 1% solutions atomized, routine shrinkage depends on response, 2% for greater constriction, for examination or hemostasis, 0.2% for displacement. Proetz, *Ann. Otol. Rhin. and Laryngol.*, 51: 112, 1942, through *J. Allergy*, 13: 429 (May) 1942.

p-AMINO HIPPURIC ACID

Mice (white)—

Toxicity: Oral dose of 2.0 gm/kg. every hour for four hours showed no toxicity. No toxicity was noticed from intraperitoneal dose of 0.2 gm/kg. sodium p-amino hippuric acid, followed by oral use of 2.0 gm/kg. hourly for four hours. Mattis et al., *J. Pharmacol. & Exper. Therap.*, 84: 147 (June) 1945.

LD₅₀: Intravenous dose, 4.93 ± 0.8 gm/kg. Ibid.

Rabbits—

Blood Concentration: Constant intravenous administration of 2.2 gm/kg. per hour to 3.2 gm/kg. per hour for six hour periods gave 604 mgm/100 ml. average six hour blood concentration, Ibid.

Dogs—

Plasma Concentration: 600 mgm/100 ml. gave rise to toxic signs when given in constant intravenous infusion. Ibid.

Man—

Plasma Penicillin Concentration: Raised through use of 6% solution of sodium salt as vehicle for intravenous administration. No important secondary effects. Beyer et al., J.A.M.A., 126: 1007, 1944.

AMINOPHENYLSTIBINATE**Man—**

Leishmaniasis Therapy. Fifteen intravenous injections of 20-200 mgm. aminophenylstibinate of methyl glucamine containing 6.5% antimony (Pentastib) controlled disease in five weeks in children under five; 50-300 mgm. in older children and adults. Course repeated two to three times; drug well tolerated but not as effective as Neostibosan. Giraud and Revol, Presse. Med., 51: 291 (June) 1943, through Trop. Dis. Bull., 41: 109 (Feb.) 1944.

AMINOPHYLLINE

(Theophylline ethylene diamine)

Rabbits and Guinea Pigs—

Bronchial Spasm Relief: 0.24-0.48 gm/10 ml. saline or glucose solution. Young and Gilbert, J. Allergy, 12: 235, 1941.

Dogs—

Experimental Coronary Occlusion: 200-300 mgm. orally, plus 120-360 mgm. orally before and/or after occlusion reduced mortality rate to 56%. Mixture of 120 mgm. aminophylline and 0.1 mgm/kg. atropine sulfate intravenous, five minutes after arterial occlusion, mortality rate in conscious dogs was 33%. LeRoy, Fenn and Gilbert, Am. Heart J., 23: 637 (May) 1942.

Postpituitary Antagonism: Intravenously, 3.4 mgm/kg. before or after injection of postpituitary solution inhibited or reduced pressor action and maintained or restored cardiac efficiency and a lower or the original blood pressure level in normal animals or in those with high blood pressure. Intravenously, 20 mgm/kg. reversed the reaction in dogs with

experimental low blood pressure, improved cardiac function which resulted in increase in blood pressure. Hanzlik and Moy, Stanford M. Bull., 3: 127 (Aug.) 1945.

Man—

Cheyne-Stokes Respiration: Intravenously 50 ml. (1.2 gm.) at 8–12 hour intervals. Death from ventricular failure one month later. Stannus and Rochie, J. Florida M. A., 28: 489 (Apr.) 1942.

Circulation Time: 1 ml. (0.24 gm.) intravenously, patient flat, end point markedly increased depth of respiration. Koster and Sarnoff, J. Lab. & Clin. Med., 28: 812, 1943.

Coronary Disease: 0.1 gm. three times daily advisable in some cases as adjuvant. Nitroglycerin given for attacks of pain. Smith, Proc. Staff Meet. Mayo Clin., 17: 307 (May) 1942.

Fatalities: Intravenous administration caused cardiac failure in two and bronchial asthma in one. One received 0.1 gm/4 ml.; another died within 30 seconds after administration of 0.25 gm/10 ml. 10% glucose. Death was sudden. Merrill, J.A.M.A., 123: 1115; 1943.

Gastric Irritation: 5% of patients (200). Roberts, Stanford Med. Bull., 2: 161 (Nov.) 1944.

Respiratory Rate: 0.48 gm. intravenously increased respiratory rate 26% and respiratory depth 51% in 22 normals. Disappearance of rhonchi and bronchial obstruction observed by intravenous use every four hours to three cases of atelectasis. Dose for prevention of postoperative respiratory complications 0.48 gm. two to three times daily in intravenous solution. Sperling, Weisman and Papermaster, Surgery, 11: 600 (Apr.) 1942.

Respiratory Depth Increased: Orally, 0.1–0.2 gm. 3–6 hourly. 90% relief of virus pneumonia (200 patients). Roberts, Stanford Med. Bull., 2: 161 (Nov.) 1944.

Colic Relief: Intravenous dose of 0.25–0.5 gm. brought prompt relief in eight patients with acute biliary pain. Gladstone and Goodman, J.A.M.A., 126: 1084; 1944.

AMINOPYRINE

Mice—

Toxicity. 300 mgm/kg. was slightly analgetic; 800 mgm/kg. caused death in four of five. Woolfe and MacDonald, J. Pharmacol. & Exper. Therap., 80: 300 (Mar.) 1944.

Man—

Rheumatic Fever: 1.5–2 gm. daily in divided doses for children; 2–3 gm. daily for adults. White cells observed weekly and drug discontinued if $< 5,000$ (see salicylates). Swift et al., New York State J. Med., 42: 895 (May) 1942.

Trench Fever (*Rickettsia quintana*): 1.2–3.0 gm. daily relieved pains in 39 of 48 patients and often seemed to control the fever but had no curative action. Jacobi, Munchen. med. Wchnschr., 89: 615 (July) 1942; through Bull. War Med., 3: 217 (Dec.) 1942.

AMINOTHIAZOLE

Man—

Hyperthyroid Therapy: 0.1 gm. given orally, four times daily for three to four weeks improved clinical symptoms without toxic effects. J.A.M.A., 129: 761; 1945.

AMMONIA

Mice—

Therapy of Poisoning: Subcutaneously, 0.1 ml. of 40% hexamine before or immediately after poisoning lowered 48 hour mortality rate to 23% and 17% respectively, as compared to 32% for controls. Boyd, MacLachlan and Perry, J. Indust. Hyg. & Toxicol., 26: 29 (Jan.) 1944.

Rabbits and Cats—

Poisoning: Symptoms described. Ibid.

AMMONIUM CHLORIDE

Man—

Alkalosis: 1 gm. ammonium chloride intravenously reduced serum carbon dioxide by an average of 1.1 volume per cent. Approximately 1,000 ml. 2% solution in 0.9% saline or 5% dextrose were given over a two-hour period. Zintel, Rhoads, and Ravdin, Surgery, 14: 728 (Nov.) 1943.

Plasma Volume: 9 gm. ammonium chloride daily for three to four days and a low-salt diet caused decrease in plasma volume and diuresis, a rise in serum proteins and hematocrit values and a water loss equivalent to 3 to 4% body weight in most of 15 patients studied. Lyons, Jacobson and Avery, Am. Heart J., 27: 353 (Mar.) 1944.

AMPHETAMINE SULFATE (Benzedrine)

Rats—

Gastrointestinal Motility: 10 mgm/kg. intraperitoneally caused 84% delay in digestion time. Smith and Penrod, Proc. Soc. Exper. Biol. & Med., 47: 418 (June) 1941.

Rabbits—

Antagonism to Alcohol: Addition of 1.5 times LD_{50} had no effect in protecting animal from LD_{50} or more alcohol, but alcohol up to 80% LD protected animal from 1.5 times LD_{50} of drug. Reifenstein, J. Lab. & Clin. Med., 27: 131 (Nov.) 1941.

Man—

Addiction: 10 mgm. four times a day gradually increased to 250 mgm. per day over a five-year period caused mental symptoms in a 49 year old man: Norman and Shea, New England J. Med., 233: 270 (Aug.) 1945.

No physical ill effects except hunger, increased restlessness and sleeplessness were observed in a patient who had taken 25–30 five mgm. tablets daily for over four years. Shorvon, Brit. M. J., II: 285 (Sept.) 1945.

Tolerance: 15–30 mgm. daily over approximately nine years, no remarkable effects. Bakst, U. S. Nav. Bull., 43: 1228 (Dec.) 1944.

Blood Changes: 10 mgm. per day for three weeks to five patients caused average increase of red blood cells of 748,000 (largest 1,250,000); hemoglobin increased average 7% (largest 15%). therefore periodic blood counts recommended for prolonged medication. Simon, M. Bull. Vet. Admin., 20: 175 (Oct.) 1943.

Fatigue: 10, 20, 40 mgm. inhibited production of voluntary muscular fatigue and abolished fatigue in exhaustion experiments. Effects on work and patellar reflex passed through a maximum two to five hours after administration. Alles and Feigin, Am. J. Physiol., 136: 392 (May) 1942.

Performance: (1) running rate improved 2.5 hours after administration of 20 mgm. of sulfate (in spite of unpleasant side effects in 71 of 250 cases). (2) ability to solve arithmetic problems decreased in non-fatigued persons by 20 mgm., increased in fatigued persons if given at dawn. Alwall, Acta. med. Scandinav., 114: 33, 1943.

Visual Acuity: 24 hours after administration of 10 mgm. average reading speed of 17 to 40 year old men improved from 0.358 seconds per letter to 0.245 seconds per letter. Visual acuity improved from 20/17.2 to 20/14.2. Even better six hours later. Superior to nikethamide (coramine). Lebensohn, Sullivan, U. S. Nav. M. Bull., 43: 90 (July) 1944.

Nervous Activity (see desoxyephedrine). Compared with alcohol had only a slight effect on motor conditional reflexes. 10-15 mgm. increased number of correct responses to negative conditional stimuli by 14% and 20-30 mgm. by 25%. 10-15 mgm. raised systolic and diastolic blood pressure 8 and 6 mm. respectively; the increase doubled by 20-30 mgm. *Resting respiration* increased 23% by 10-15 mgm. and 20% by 20-30 mgm., but *resting pulse rate* not affected. Acuity to hearing and threshold of sensitivity of palmar surface to electric shock were not changed. Subjects became more alert and wide awake. Finkelstein, Alpern and Gantt, Bull. Johns Hopkins Hosp., 76: 61 (Feb.) 1945. (See alcohol.)

Inhalation of 5% Mists: Effects lasting over two hours diminution of hourly pulmonary ventilation, slowing of respiratory rhythm, increase of volume in each respiration, increase of pressure of carbon dioxide in expired air, fall in pressure of carbon dioxide in alveolar air, rise in alveolar oxygen pressure. Dautrebande et al., Arch. internat. de pharmacodyn. et de therap., 66: 337 (Sept. 30) 1941.

Alcoholism: 10 mgm. twice a day plus 30-40 mgm./day thiamine chloride and 0.1 gm. phenobarbital interrupted acute alcoholic cycle in 49 of 56. Amphetamine as adjuvant to psychotherapy. Miller, Am. J. Psychiat., 100: 800 (May) 1944.

Coronary Occlusion: Overcame untoward effect of 0.030-0.05 gm. morphine by 10-20 mgm. benzedrine sulfate. Repeat 10 mgm. four hours later. Maximum dose 40 mgm. Guyot, J. Missouri M. A., 38: 93 (Mar.) 1941.

Dysmenorrhea: 10 mgm. orally relieved 45 of 55 patients of cramps. Brown, J. Missouri M. A., 39: 253 (Aug.) 1942.

Irradiation Sickness. 5-10 mgm. oral, 30 minutes after breakfast, at noon and 4 p.m. from start of x-ray sickness until three days after last roentgen treatment. Daily dose never exceeded 30 mgm. 21/27 definite remission. Jenkinson and Brown, Am. J. Roentgenol. 51: 496 (Apr.) 1944.

Schizophrenia. 10 mgm. intravenously caused talkativeness, restlessness and tension in four, no reaction in six. Gottlieb and Coburn, Arch. Neurol. & Psychiat., 51: 260 (Mar.) 1944.

Corrective to Sedative in Epilepsy. 5-30 mgm. oral daily. Robinson, Am. J. Psychiat., 98: 215 (Sept.) 1941 through J. A.M.A., 118: 80 (Jan. 3) 1942.

Urticaria. 2.5 mgm. every three to five hours relieved six children, and two who did not respond were relieved with 5 mgm. every four hours. Roberts, J. Florida M. A., 32: 193 (Oct.) 1945.

ISO AMYL AMINE

Guinea Pigs—

Normal Blood Concentration: Less than 1 p.p.m. of amines. Richter, Lee, and Hill, *Biochem. J.*, 35: 1225, 1941.

Man—

Detoxification Rate: 60–250 mgm/kg. per hour when 500 mgm. were injected intravenously. *Normal human blood concentration* was less than 1 p.p.m. *Ibid.*

ISOAMYLHYDROCUPREINE (Eucupine)

Man—

Acute Iridocyclitis Treatment: 0.5 ml. of a mixture (containing 30 ml. of 1:500 concentration isoamylhydrocupreine di-hydrochloride in 1% procaine hydrochloride plus 0.5 ml. of epinephrine) injected at site of supraorbital nerve as it leaves the orbit through the supraorbital notch. Richter, *Arch. Ophth.* 27: 579 (Mar.) 1942.

Migraine: Infiltration of the superficial temporal artery of the involved side with 2 ml. of 0.1% Eucupine in 1% procaine hydrochloride was effective in four of five. Patzer, Derbes and Engelhardt, *Arch. Surg.*, 50: 296 (June) 1945.

Man—

AMYL NITRITE

Pulmonary Cerebral Effect Time: A three minim pearl was inhaled slowly and deeply for two minutes and then subject breathed normally again. The subject signaled immediately on perception of sensory change. Measurements were between 10 and 16 seconds and averaged 12 seconds. The method measured the effective pulmonary ventilation and the circulation time of the left side of the heart. Uhley, *J. Lab. & Clin. Med.*, 27: 1111 (June) 1942.

Man—

AMYL SALICYLATE

Mustard Gas Burns: Applied undiluted helped to dry up the exudation, reduced surrounding edema and erythema and diminished pain, irritation and discomfort. Great Britain Ministry of Health, Emergency Medical Services Instruction, Part I. Medical Treatment and Special Centres Supplement, 43, July, 1942: through *Bull. War Med.*, 3: 170; 1942.

AMYTAL SODIUM

(Sodium-5-ethyl-5-isoamyl-barbiturate)

Man—

Psychiatric Uses: Intravenously, less than 0.5 gm. at maximum rate of 0.1 gm. per minute in patients with marked hypertension, obvious myocarditis, and pulmonary infection or edema; larger dose given to patients without complications. Used in sedation of disturbed, uncooperative, or epileptic patients; and amelioration of catatonic excitements and termination of manic episodes by narcosis technic; hypnosis of patients not responding to ordinary psychotherapy hypnosis; and in stimulating doses, differential diagnosis between manic and catatonic stupor, between schizophrenic mutism and hysterical amnesia and aphonia, between organic and functional psychoses, and between cases which can and cannot be expected to respond to insulin shock. Sullivan, *Am. J. Psychiat.*, 99: 411 (Nov.) 1912.

Schizophrenia. 250 mgm. given intravenously caused five of ten to be friendly, three of ten moderately improved and two of ten showed poor reaction. Duration of action 3.9 hours. Gottlieb and Coburn, *Arch. Neurol. & Psychiat.*, 51: 260 (Mar.) 1944.

War Neuroses: 200–300 mgm. intravenously, two to three times weekly for purpose of narco-suggestion or narco-catharsis; psychogalvanometric readings to diagnose tension states. Hoch, *Bull. New York Acad. Med.*, 20: 333 (June) 1944.

Battle Stress: 7.2 gm. was given for average narcosis of ten days' duration. Rome, *U. S. Naval M. Bull.*, 42: 525 (Mar.) 1944.

Intelligence Test: 0.2 gm. lowered I. Q. average 3.36 points. Slater, Sargent and Glen, *Lancet*, 242: 676; 1942.

Uterine Contractions in Labor. 0.54 gm. had no effect on amplitude, diminished tonus. Bickers, *Virginia M. Monthly*, 69: 15 (Jan.) 1912.

ANGIOTONIN

(Hypertensin)

Frogs—

Vasoconstriction Intravenously, 5 to 10 ml. resulted in temporary hypertension in man. Ultrafiltrates of citrated blood plasma from these persons caused greater vasoconstriction in pithed animals than did ultrafiltrates from normotensive or hypertensive persons. Perfusion with 1:500 dilutions in phosphate buffered calcium free frog Ringer's solution (pH 8.3) always produced vasoconstriction. Gregory et al, *Arch. Int. Med.*, 76: 11 (July) 1915.

Guinea Pigs—**ISO AMYL AMINE**

Normal Blood Concentration: Less than 1 p.p.m. of amines. Richter, Lee, and Hill, *Biochem. J.*, 35: 1225, 1941.

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ANTERIOR PITUITARY EXTRACT

Rats (female)—

Growth Hormone: 0.01 mgm. per day of growth hormone from oxen given intraperitoneally for ten days starting fourteen days after hypophysectomy caused 10 gm. weight increase. 5 mgm. produced no lactogenic, thyrotropic, adrenocorticotropic, follicle-stimulating or interstitial cell stimulating effects. Li and Evans, Science, 99: 183; 1944.

Man—

Diabetic Dwarfism in Children: 3 ml. intramuscularly were given every second day and thyroid U.S.P. 0.065–0.2 gm. (1–3 gr.) a day. Wagner, White and Bogan, Am. J. Dis. Child., 63: 661 (Apr.) 1942.

Spermatogenesis: Orally 4.8 gm. daily for six months or less never failed to improve or cure patient with deficient spermatogenesis. Huhner, Am. J. Obst. & Gynec., 47: 144 (Jan.) 1944.

ANTHIOMALINE

(Lithium antimony thiomalate)

Man—

Microfilaria: 85–100% reduction of *W. bancrofti* in blood with 180 mgm. daily for seven to twenty-eight days (total 0.9–4.59 gm.). Vomiting with epigastric pain after total dose of 0.78–1.89 gm. Brown, J.A.M.A., 125: 952 (Aug. 5) 1944.

ANTIBIOTICS*

Urethane, p-aminobenzoic acid: Antagonistic to sulfonamide action on growth and luminescence of luminous bacteria *Cypridina*. All agents acted in same way as narcotics on luminous bacteria; stimulated growth and luminescence in low concentrations and inhibited in high concentrations. Stimulative action of one may antagonize or completely overcome inhibitory effect of another that was simultaneously present. This anti-sulfonamide action may well be due to stimulating effects of antagonists in low concentrations on bacteria rather than any competitive action as previously postulated to exist between them. Johnson, Science, 95: 104 (Jan. 23) 1942.

*Only data pertinent to the experimental laboratory have been included in this survey (see penicillin, streptomycin and other antibiotics under their respective names) Annotated bibliographies are currently published at frequent intervals by others.

Assay—

Agar-streak Method: Proved rapid, did not require a sterile sample, permitted the simultaneous testing of unknown substances against several bacteria or fungi, and was applied to nonaqueous solutions. The results were expressed in dilution units that amount of material which, added to 1 ml. of test medium, just inhibited the growth of the test organism = 1 unit. Waksman and Reilly, *Indust. & Engin. Chem., Anal. Ed.*, 17: 556 (Sept.) 1915.

Canaries—

ANTIMALARIALS*

A series of antimalarials prepared by reacting 8-(γ chloropropyl amino)-6-methoxyquinoline with various primary and secondary bases to give 8-(substituted amino) propyl amino-6-methoxy quinoline. Maximum tolerated dose and minimum effective dose in mgm/20 gm. was determined on canaries. Most potent of compounds, 8-[γ (tertiary butyl-amino) propyl amino]-6-methoxy quinoline (R. 109) was equal to pamaquin (Plasmoquin) against *Plasmodium relictum* in canaries. Crum and Robinson, *J. Chem. Soc.*, 561 (Nov.) 1943; Quin and Robinson, *Ibid*, 555 (Nov.) 1943; Glen and Robinson, *Ibid*, 557 (Nov.) 1943.

Chicks—

Screening Method: Six-day old chicks, acutely infected with *Plasmodium gallinaceum*, were given compound to be tested on same day and then twice a day, or three times a day, on next three or four days, in 1 ml. solution or suspension by catheter directly into gizzard. Activity was judged from blood smears taken at peak of parasitemia. Curd, Davey, and Rose, *Ann Trop Med*, 39, 139 (Dec) 1945.

*For more complete chemical and pharmacologic data consult Survey of Antimalarials, 1941-1945 by F. Y. Wiselogle, Edwards Bros., Ann Arbor, Michigan

Man—

ANTIMONY

Schistosomiasis Therapy. Intravenous dose of 8 ml. 0.5% solution antimony potassium tartrate initially, if tolerated, subsequent doses on alternate days increased in amounts of 4 ml per dose until 28 ml. dose had been reached. A total of 360 ml was maximum. U. S. War Dept. Tech Med. Bull, 167 War Med 397 (June) 1945.

Asiatic Schistosomiasis. Intravenously, 0.03-0.15 gm. antimony potassium tartrate in 1% solution in gradually increasing amounts every

second day to a total of 1.95 gm. in approximately one month were given to 42 patients at the rate of 1 ml. per minute for the first three doses and subsequently in one liter of 5% dextrose solution allowing one hour for injection. Intramuscularly, 1.5 ml., 3.5 ml., and then 5.0 ml. doses were given on alternate days to a total of 50 ml. to 20 patients. Both methods were effective. Johnson and Berry, War Med., 8: 156 (Sept.) 1945.

Granuloma Venereum Therapy: Trivalent antimonial compound (Diramin) injected every five days, 1 ml. (8.5 mgm. antimony) initially increased to 5 ml. Paggi and Hull, Ann. Int. Med., 20: 686 (Apr.) 1944.

Schistosomiasis: Cure without recurrence in one case. Initial intravenous dose of 0.03 gm. antimony potassium tartrate in 5 ml. saline, increased by 0.03 gm. daily until 0.1 gm. was given. Later, seven injections intravenously of 0.13 gm. at 48 hour intervals. Hogarth, Canad. M. A. J. 50: 253 (Mar.) 1944.

Mice (albino)—

Toxicity and Efficacy: LD₅₀'s (mgm. antimony per kg.) were determined for 32 compounds. Efficacy was determined as the ratio of number of treatments required at 0.8 mgm. antimony per kg. to the LD₅₀ value. Lawton et al., Am. J. Trop. Med., 25: 263 (May) 1945.

Rats (Cotton)—

Litomosoides carinii: Five compounds, given intramuscularly at 3.3 mgm. of antimony per kg. were well tolerated and effective in killing adult parasites. Ibid.

Dogs—

Experimental Filiarisis: Six intravenous doses per week of 0.8 mgm. antimony per kilogram was successful schedule in eliminating microfilariae from the peripheral circulation in 28 of 29 dogs with 16 antimonyl compounds and antimonous oxide. Infection with *Dirofilaria immitis*. Lawton et al., Am. J. Trop. Med., 25: 263 (May) 1945.

ANTIMONY SODIUM MANNITE

Hamsters (Chinese)—

Kala Azar: Five of six freed of *Leishmania donovani* with subcutaneous injection of 12.5 ml. 30% solution per kg. twice a day at 10 to 12 hour intervals for 36 days. Total of 900 ml. containing 56.7 gm. antimony per kg. Chung and Chow, Chinese M. J., 62: 26 (Jan.-Mar.) 1944.

Routes of Administration: Intramuscular, intravenous or subcutaneous Ibid.

Toxicity: Maximum nonlethal dose: 30 ml. 30% solution; M.L.D.: 70 ml. 30% solution; universal lethal dose: 120 ml. 30% solution. Lethal doses caused hydropic degeneration of liver and degenerative changes in renal tubules. Ibid.

ANTIVENIN

Man--

Blackwater Fever: 200 ml. 1:300 solution, initially, and 10 ml. every four hours thereafter aborted attacks of blackwater fever in 36. Singh and Singh, *Nature*, 154: 84 (July) 1944.

ANTUITRIN-S

Man--

Migraine Therapy: 75 rat units, followed by 100, 150, 200 units at four to six day intervals followed by 200-300 units once or twice weekly for two weeks. Then 250 units weekly were given for one month, continuing with 250-300 units monthly for two months. Fifteen of thirty lost headaches and symptoms entirely. Leyton, *Lancet*, 242: 488 (Apr.) 1942.

APOMORPHINE

Man--

Paroxysmal Tachycardia: Relief obtained immediately by administration of 3-6 mgm. subcutaneously. Nausea within five minutes then vomiting and patient relaxed. Needels, *U. S. Nav. Med. Bull.*, 42: 1282 (June) 1944.

ARSENICALS

Determination in Fluids and Tissues: Organic matter was destroyed and arsenic was precipitated as the iron-free magnesium ammonium arsenate. Metallic arsenic was precipitated from this compound, dissolved in hydrochloric acid, treated with iodine and finally titrated with hyposulfite. Lespagnol, Merville and Werquin, *Bull. Soc. chim. biol.*, 25: 322, 1943.

Photometric Determination for arsenic, copper, zinc and iron in organic medicinals. Strafford, Wyatt and Kershaw, *Analyst*, 70: 232 (July) 1915.

Rats—

Detoxication: Lethal effect of an intraperitoneal dose of 450 mgm/kg. arsanilic acid or 1,500 mgm/kg. carbarsonc was inhibited by previous administration of o- and m-aminobenzoic acid and by nitro-, hydroxy-, and methyl analogues. Sandground, J. Pharmacol. & Exper. Therap., 80: 393 (Apr.) 1944.

Rabbits—

Blood Arsenic: One minute after injection of phenyl arsenoxide, 3-amino-4 ethanol phenyl-arsenoxide, 3-amino-4 hydroxyphenyl arsenoxide, and tryparsamide, having relative molar toxicities of 100, 44, 7.9, and 0.09 respectively, the per cent of blood arsenic in the red blood cells was >95, 75-95, 25-75, and 5, respectively. Hogan and Eagle, J. Pharmacol. & Exper. Therap., 80: 93 (Jan.) 1944.

Man—

Occupational Exposure: 0.006-0.5 mgm. arsenic trioxide per 100 ml. urine excreted was reduced to 0.02-0.09 mgm. arsenic trioxide per cent after dust control measures were adopted. Watrous and McCaughey, Indust. Med., 14: 639 (Aug.) 1945.

Relapsing Fever (tick borne): Maximum dose 3.45 gm. arsenic given intravenously. Pyrexial relapse in 4 of 63 cases. Cooper, Med. J. Australia, 1: 635 (June) 1942.

Syphilis Therapy: One to three injections of 0.25-0.5 gm. of 4,4'-dihydro-arsenobenzene-3,3'-bis((azo-2)-naphthol-1-disulfonic acid-4,8) given. Friedheim, Argentine Assoc. Dermat. and Syph. through J.A.M.A., 116: 2331 (May 17) 1941.

ARSENO-BISMULAK

(Sodium p-aminophenylarsonate and bismuth subgallate)

Rats—

Absorption and Distribution. Intramuscular injection of 0.041-0.564 ml/kg. were completely absorbed within one to four hours and rapidly distributed to tissues. Both metals found one week after last injection. Bismuth found in muscle and brain of 61% of animals. Lehman, Craver, and Chase, Urol. and Cutan. Rev., 48: 229 (May) 1944.

LD: 0.5 ml/kg. intravenously, or 1.25 ml/kg., intramuscularly. *Tolerated:* 0.2 ml/kg. intravenously. Bruce et al., Urol. & Cutan. Rev., 48: 183 (Apr.) 1944.

Rabbits—

LD: 2.0 ml/kg., intravenously. *Tolerated*: 0.2 ml/kg (1.56 mgm arsenic plus 2.1 mgm. bismuth). 60% *Fatal Dose*: 0.2 ml/kg, intramuscularly. *Ibid*.

Dogs—

Fatal 1.25 ml/kg., intramuscularly. *Tolerated*: 0.2 ml/kg, intravenously. *Ibid*.

ARSENOXIDE HYDROCHLORIDE

(m-amino-p-hydroxyphenyl arsenious oxide-hydrochloric acid)

Man—

Syphilis: 12 gm. for men, 0.8 gm. for women by intravenous drip therapy. Solvents were isotonic dextrose or physiologic sodium chloride. Prats, Varas, and Haraszt, *Arch. Dermat. & Syph.*, 45: 885 (May) 1942.

 γ -(p-ARSENOSOPHENYL)-BUTYRIC ACID

Stability: Neutral solution of sodium salt sterilized by autoclaving kept in sealed ampules 12 months at room temperature without change. Eagle, *Science*, 101: 69 (Jan. 19) 1945.

In Vitro: *Trypanosoma cruzi* killed by concentrations above 1:400,000 in four hours. *Ibid*.

Man—

Curative Dose. In early trypanosomiasis without central nervous system involvement approximately 0.4 mgm/kg. daily for less than two weeks was effective. *Ibid*.

Tolerated: Intravenous injections of 2% sterile solution daily or two to three times a week, total of six to 24 injections. Dose 0.25–0.5 mgm/kg. (more than 800 injections). *Ibid*.

Trypanosomiasis: 40 mgm. thrice weekly to a total of 360 to 400 mgm. caused blood and lymph nodes to become negative in seven patients with early infection and neurologic involvement. Weinman and Franz, *Am. J. Trop. Med.*, 25: 313 (July) 1945.

ARSONIUM COMPOUNDS

Rats—

Trimethyl-3-amino-phenylarsonium chloride:

M.T.D., 30 mgm/kg, M.L.D., 40 mgm/kg

Intravenous injection of 10 mgm/kg. was no protection against *Trypanosoma equiperdum* infection. Blicke and Safir, *J. Am. Chem. Soc.*, 63: 1493 (June) 1941.

Trimethyl-3-amino-4-hydroxyphenylarsonium chloride:

M.T.D., 70–80 mgm/kg.; 50 mgm/kg. had no trypanocidal effect; 1:100 concentration had no germicidal action. *Ibid.*

Tetra-(4-aminophenyl) arsonium chloride:

M.T.D., 20 mgm/kg.; M.L.D., 30 mgm/kg.

Intravenous injection of 10 mgm/kg. was no protection against *Trypanosoma equiperdum* infection. *Ibid.*, 63: 1496 (June) 1941.

ARSPHENAMINE**Rabbits—**

Experimental Syphilitic Orchitis cured by single dose 0.04–0.06 gm/kg. orally. 0.08 gm/kg. neoarsphenamine. M.C.D., 0.012 gm/kg. intravenously; 0.02 gm/kg. neoarsphenamine.

Repeated dose, oral: 0.02 gm/kg. orally for five days. 0.04 gm/kg. five days neoarsphenamine, effected biologic cure. Kolmer, Brown, and Rule, *Am. J. Syph., Gonorr. & Vener. Dis.*, 26: 63 (Jan.) 1942.

Man—

Early Syphilis: 2% solution three to four times a day for five to six days, total dose increased from 1.5 gm. in early cases to 4.4 gm. in later cases. Dark field test negative within 24 hours after first injection. 118 of 178 (66%) followed for three months to three years remained serologically and clinically negative. Cannon et al., *J.A.M.A.*, 126: 544; 1944.

Massive arsenotherapy: Intravenously, 4 gm. over five days with 81% satisfactory results. Leifer, Chargin, and Hyman, *J.A.M.A.*, 117: 1154; 1941.

Seven intravenous injections of 0.6 gm. at daily intervals (total 4.2 gm.). Kolmer and Rule, *Arch. Dermat. & Syph.*, 44: 1055 (Dec.) 1941.

Intravenously administered dose of arspenamine or neoarsphenamine in the morning, intravenous solution of 1 gm. sodium thiosulfate at noon, intravenous solution of 2–4 gm. sodium iodide in the evening. Treatment for 4 successive days. No solid food, 0.5 gm. tablets sodium thiosulfate, eight tablets; fluids forced. Excellent results. Goodman, *Urol. & Cutan. Rev.*, 46: 378 (June) 1942.

ASCORBIC ACID**Assay—**

Ultraviolet Spectrography Method was superior to p-dichlorophenol indophenol assay because of its specificity, possibility to draw quantitative conclusions and to determine the equilibrium between ascorbic and

dehydroascorbic acid. Halden and Schauenstein, *Naturwissenschaften*, 30: 586, 1942; through *Die Chemie*, 55: 349 (Nov.) 1942.

Content in Tumor Tissues: 15-70 mgm/100 gm. fresh tissue in 22 tumors. Content not related to origin, rate of growth, age of host nor site of transplantation. Robertson, *J. Nat. Cancer Inst.*, 4: 321 (Dec.) 1943.

Clinical Estimation—

Obtained by bubbling coal gas through oxalated blood, treating with metaphosphoric acid and sodium acetate, centrifuging, and titrating the supernatant fluid with 2,6 dichlorophenolindophenol. Duny, Murdock, and Rogan, *Biochem. J.*, 36: 271 (Apr.) 1942.

Reduction of Methemoglobin—

Ascorbic acid at pH 7 and 0° C. reduces methemoglobin 80 to 90% within six hours. When carried out at room temperature with methylene blue, interaction is complete in one hour between two systems. Vestling, *J. Biol. Chem.*, 143: 439 (Apr.) 1942.

Chicks—

Growth: 100 mgm/100 gm. purified ration containing solubilized liver stimulated growth to a small but definite extent. Briggs et al., *Proc. Soc. Exper. Biol. & Med.*, 55: 130 (Feb.) 1944.

Mice—

Liver Ascorbic Acid Content: 322-467 microgram/gram in both sexes of three high-cancer strains, 344-356 in males of low cancer, pure CBA strain, 219-307 in females of CBA strain, 175-216 in both sexes of low cancer, pure C57 strain, and 185-224 in buff MRC and stock mice. Kennaway, Kennaway and Warren, *Cancer Research*, 4: 245 (Apr.) 1944.

Mice, Rabbits—

Action on *Treponema pallidum*: Subcutaneously, 100 mgm. mixed with a suspension of treponema had no pathogenic activity. 0.002 gm. did not suppress pathogenicity. Levaditi and Pérault, *Compt. rend. Soc. de biol.*, 139: 7 (Jan.) 1945.

Rats—

Survival in Trauma. Subcutaneously, 100 mgm/kg saved the rats' supply of ascorbic acid. Ungar, *Nature*, 149: 637 (June) 1942.

Guinea Pigs—

Storage: 1.5-100 mgm. daily were given for 20 days to animals on vitamin deficient diet and then withheld. Average survival time ranged from 1.7 days when 1.5 mgm. were given to 28 days for animals that

received 100 mgm. It was concluded that ascorbic acid was not stored. Giroud et al., Bull. Soc. chim. biol., 25: 144 (Apr.-June) 1943.

Experimental Bone Injuries: Subcutaneous, 0.25-4.0 mgm. daily showed that at least 2 mgm. daily required for normal bone regeneration. Bourne, J. Physiol., 101: 327 (Nov.) 1942.

Experimental Tuberculosis: Better general condition, greater increase in weight and prolonged life with 2.5, 5.0 and 10.0 micrograms in diet than with only 0.5 and 1.0 micrograms daily. Kleimenhagen, Ztschr. f. Vitaminforsch., 11: 209; 1941.

Survival in Injury: Subcutaneous > 100 mgm/kg. saved animal; otherwise 100% death. Time-delay of one hour reduced survival to 50%. Ungar, Nature, 149: 637 (June) 1942.

Wound Healing. Abdominal scar with 0.31 mgm/100 gm. vitamin C content required 70 mm. Hg pressure for skin separation and 127 mm. Hg for wound rupture. High vitamin C diet scar with 7.64 mgm/100 gm. vitamin C content, 140 mm. and 258 mm. Hg respectively needed for skin separation and wound rupture. Bartlett, Jones, Ryan, New England J. Med., 226: 469 (Mar.) 1942.

Dogs—

Anesthesia. Ascorbic acid reached its highest plasma concentration in anesthetized dogs within seven hours of induction with vinethene or ether and at end of anesthesia with chloroform. Beyer, Stutzman, and Hafford, Surg., Gynec. & Obst., 79: 49 (July) 1944.

Calves—

Dermatosis: (with low ascorbic acid blood levels) Subcutaneous dose of 3 mgm. ascorbic acid initially and feeding of 1 gm chlorobutanol daily effective. Cole, Rasmussen, and Thorp, Vet. Med., 39: 204 (May) 1944.

Cows—

Utilization: < 100 mgm. daily in a diet for 15 months maintained normal physical condition and the animal gave birth to a normal calf. Excretion: 258 mgm. daily in the milk and 57 mgm. in the urine during four months when the average intake was 99.7 mgm per day. Vavich et al., J. Dairy Sci., 28: 759 (Oct.) 1945.

Sterility Therapy: Given 2 gm. subcutaneously on first day of heat, bred immediately, and then given 2 gm. every three days for three weeks. Phillips, Natl. Research Council, Committee on Animal Nutrition, Third Report, J. Am. Vet. M. A., 103: 386 (Dec.) 1943.

Horses and Cows—

Low Fertility Treatment: 1.0–1.5 gm/500 kg weight two times weekly. Clark, Davis, and Haffman, Mich. State Coll. Post-grad. Conference 1912; through M.S.C. Vet., 2: 43; 1942.

Bulls—

Sterility Therapy: Subcutaneous dose of 2 gm. every three to four days for two to six weeks was effective. Ibid.

Horses and Swine—

Sterility Therapy. Addition of 2 gm. per 500 kg. weight was effective. Ibid.

Ewes—

Blood Values: 0.43–0.82 mgm/100 ml.

Colostrum Value: 2.01–9.94 mgm/100 ml.

Milk Values: 0.38–1.77 mgm/100 ml. after fifth or sixth day following lambing. Satterfield et al., J. Nutrition, 24. (Aug.) 1912.

Monkeys—

Chronic Deficiency Anorexia, loss of weight, loss of hair, hemorrhage of the gingiva and other tissues, inability to walk because of joint hemorrhage, and finally ankylosis of knee joints. Average dose of 1.96 mgm. daily for 208 days was sufficient to protect seven growing monkeys weighing 3.64 kg. or less from scurvy symptoms. Combined calcium and ascorbic acid deficiency led to additive rather than synergistic effects. Fraser, Pub. Health Rep., 57: 959 (June) 1912.

Deficiency Treatment Gingivitis and periodontal disease treated with intramuscular dose of 30 mgm. with prompt arrest of symptoms in early stages of inflammatory and gingival hemorrhage. 3–6 mgm. doses consistently improved general condition as well as mouth lesions. Ibid., 57: 968 (June) 1912.

Pathology Tomlinson, Ibid., 57: 987 (July) 1912.

Man—

Requirement Age 5–13 40–50 mgm. gave blood levels indicative of liberal intake Bessey and White, J. Nutrition, 23: (Feb. 20) 1912.

Requirements in Children 7–12 years. 1.7–2.4 mgm/kg body weight was sufficient to (a) maintain a blood level above 0.7 mgm. per 100 ml.; (b) provide for maintenance of average "retention" value; (c) insure saturation on basis of a 50% excretion of a 300 mgm. test dose Roberts and Roberts, J. Nutrition, 21 (July 10) 1912.

Requirement: 100 mgm. per day for very young adults and < 100 mgm. for adults between 25-50 years. Purinton et al., J. Nutrition, 26: 509 (Nov.) 1943.

Saturation maintained with daily 50 mgm. intake in addition to approximately 20 mgm. in diet for ambulatory patients. Goldsmith, Ogaard, and Gowe, Arch. Int. Med., 67: 590 (Mar.) 1911.

Requirement: 62-72 mgm. for pre-adolescent girls 6-12 years. Roberts et al., J. Nutrition, 26: 539 (Nov.) 1942

Proc. Soc. Exper. Bi.

Optimal Plasma Level: To maintain 0.8 mgm/100 ml. plasma: gave 0.8-1.2 mgm/kg. body weight (averaging 1.0 ± 0.14 mgm.). Fincke, Landquist, and Carpenter, J. Nutrition, 23: (May 11) 1912.

Plasma Concentration: 65-150 mgm. supplements required to maintain tissue saturation. Storvick and Hanck, J. Nutrition, 23: (Feb. 10) 1942.

Plasma Levels: Levels > 0.8 mgm/100 ml. suggested intake exceeding body requirements; levels of not < 0.4 mgm/100 ml. indicated a sufficient C intake. At least 60 mgm. per day were required to maintain latter level. Prunty and Vass, Biochem. J., 37: 623; 1943.

Blood Plasma Levels: 0.67 mgm.% for younger and 0.81 mgm.% for older college women. Dodds and MacLeod, J. Nutrition, 27: (Apr.) 1944.

Synthesis in Infants: C content of spinal fluid remained at level of 7 mgm.% (average) in healthy even when deprived of vitamin C. Ability to synthesize during first ten months of life, falls off at 11 months and lost at one year. Rohmer and Bezssonoff, Ztschr. f. Vitaminforsch., 12: 104; 1942.

Absorption from Small Intestine: Absorption of ascorbic acid solution comparable in subjects. Absorption of ascorbic acid, the same for both. Absorption of ascorbic acid terminated at 45 cm. was of same degree as segment terminated at 90 cm. beyond point of instillation. 188-374 mgm. (31-62%) absorbed. Nicholson and Chornock, J. Clin. Investigation, 21: 505 (July) 1942.

Saturation Test: Adequate intake is indicated by ascorbic acid excretion of approximately 20 mgm. or more in four hours or approximately 30 mgm. or more in six hours following oral dose of 200 mgm. ascorbic acid. Engelfried and McWilliams, J. Lab. & Clin. Med., 29: 324 (Mar.) 1944.

"Utilization" Values: 1 mgm/kg. body weight. An intake of 1 mgm/kg. increased plasma ascorbic acid in all subjects. Dodds et al., J. Nutrition, 27: (Jan.) 1944.

Urinary Excretion: Intravenous injection of 200 mgm. caused excretion of 29.4 mgm. total ascorbic acid and 24.2 mgm. reduced ascorbic acid in urine in six hours. The measurement of either substance proved suitable for determination of relative load test response. Berryman, French, and Harper, J. Nutrition, 27: (Apr.) 1944.

Excretion in Feces. 3.8-4.46 mgm. determined by method of Shinn and Farmer. Intravenous administration increased this amount but not oral administration. Martin, Klin. Wchnschr., 20: 287; 1941.

Selective Filtration by Placenta: In seven Newfoundland women at parturition, C content was higher in cord blood plasma than in maternal blood. McDevett et al., Proc. Soc. Exper. Biol. & Med., 51: 289 (Nov.) 1942.

Diuretic Effect: Oral 500 mgm. ascorbic acid daily for six days increased average urinary output from 250 ml. to one liter every 72 hours in ten patients. Intravenously, negligible increase resulted. Daily use of two ml. Mercupurin with 500 mgm. ascorbic acid increased average urinary output in 15 of 20 patients from 0.5-2.0 liters in 24 hours with a smaller output in five. Diuresis was 0.5-2.5 times greater than with Mercupurin alone. Shaffer, J.A.M.A., 124: 700; 1944.

Deficiency Treatment: Pre-therapy-24 hour ascorbic acid excretion was 2-11 mgm.; basic plasma levels were 0-0.39 mgm%. Plasma ascorbic acid level was 1.11-1.91 mgm % on the first day that urinary excretion exceeded 40 mgm. Total dose required to bring excretion to normal level was 0.5-2.0 gm. (average 1.28 gm.). Amount required for saturation was 1.5-2.8 gm. Kyhos, Sevringhaus, and Hagedorn, Arch. Int. Med., 75: 407 (June) 1945.

Scurvy Treatment. 50-500 mgm. daily. Immediate and complete recovery in 13 children. Moise, North Carolina M. J., 3: 290 (June) 1942.

Vitamin C Deficiencies Effect of large doses studied. 100-500 mgm. single dose; excellent if plasma level low. Amount required for saturation 1.5-2.8 gm. Kyhos, Sevringhaus, and Hagedorn, Arch. Int. Med., 75: 407 (June) 1945.

Detoxifying Action of Ascorbic Acid in Arsenic Therapy: Maintained high level of vitamin C in blood to inhibit toxic products of oxidation. Patients hazardous for desensitization to neoarsphenamine by means of ascorbic acid gave positive reaction to a patch test of 30% neoarsphenamine.

mine plus 10% ascorbic acid. Bundesen et al., J.A.M.A., 117: 1692 (Nov. 15) 1941.

Arsenical Detoxication: Cutaneous reaction upon patch testing with 30% solution of neoarsphenamine could be prevented by addition of 10 or 20% ascorbic acid to solution used. Abt, U. S. Naval Med. Bull., 40: 291 (Apr.) 1942.

Treatment of Arsenical Dermatitis: Oral and intravenous 300 mgm. daily. Delp, J. Kansas M. Soc., 42: 519 (Dec.) 1941.

Sulfonamide Allergy: 500 mgm. daily affected return to normal of six patients. Normal urinary excretion of ascorbic acid was doubled in ten healthy students given sulfathiazole for four days. Holmes, Ohio State M. J., 41: 923 (Oct.) 1945.

Abortion: Habitual, spontaneous and threatened abortion patients treated with high vitamin C diet plus 100 mgm. ascorbic acid daily, high vitamin K diet and synthetic vitamin K plus mineral supplement which provided iron, copper, cobalt, nickel, and zinc plus alpha tocopherol 240 mgm. monthly. Javert and Stander, Surg., Gynecol. & Obst., 76: 115 (Jan.) 1943.

High-color Index Anemia: Intramuscular injections of 9.1–11.2 gm. in 13 to 16 days improved three patients. Gottlieb, Brit. M. J., II: 119 (July) 1945.

Bone Regeneration: 20–40 mgm. daily may be required; 40 mgm. given daily for fractured bones. Bourne, J. Physiol., 101: 327 (Nov.) 1942.

Upper Respiratory Tract Infection: Plasma ascorbic acid levels below 0.2 mgm.% in 19 patients with persistent colds, sore throat, etc. were given 100–400 mgm. per day for 10 to 14 days, then 50–100 mgm. per day for one month. This relieved congested nose, red and shiny pharynx, cracked lips and excoriated nostrils. Macbeth, Proc. Roy. Soc. Med., 36: 625 (Sept.) 1943.

Colds: 100–200 mgm. daily did not significantly decrease the incidence, duration and severity of colds. 774 college students over two years. Cowan, Diehl, and Baker, J.A.M.A., 120: 1268; 1942.

Epistaxis: Certain cases treated with 1 gm. intravenously. If no result, 0.5 of whole dose repeated after few minutes. When hemorrhage ceased, dose was repeated four or five hours later and 0.5 dose administered daily thereafter for several days. Tieffenberg, Semana Med., 49: 312; 1942; through Quart. Rev. Otorhinolaryngol., 1: 70 (Mar.) 1942.

Epinephrine Sensitivity: Intravenously 500 mgm. daily until blood and urine showed high amounts. Blood pressure elicited with epine-

phrine was higher than normal. In some, thrombocytes also increased. Molnar and Fridrick, *Klin. Wchnschr*, 20: 1079; 1941.

Gastric and Colonic Surgery required 2000-3000 mgm. given before operation for sufficient tensile strength of wounds. Graham, *Brit. M. J.*, I: 335 (Mar.) 1912.

Renal Hypertension 150 mgm. per day with 1 gm. ammonium chloride three times a day for 10 to 15 days with a five-day rest potentiated treatment. 150-1000 mgm. produced tachycardia, uneasiness and anxiety in the hypertensive. Schneider, *J. Nerv. & Ment. Dis.*, 99: 936 (June) 1914.

Tropical Ulcer: Intramuscularly, 200 mgm. every other day for two weeks. Brown, *Bull. U. S. Army Med. Dept.*, 89: 14 (June) 1915.

Typhoid: Treated with 1200 mgm daily without toxicity (400 mgm. parenteral, 800 mgm. oral) Cements endothelial cells of capillaries and thus decreases permeability of capillaries; stimulates bone marrow to produce more platelets; has coagulation promoting effect; raises production of antibodies; heals ulcers. Drummond, *Proc. Cape Town Med. A.*, (Aug) 1913; abstr *Clin. Med.*, 52 173 (May) 1915.

Vaginal Ulceration healed with 300-500 mgm. ascorbic acid daily. Patient with vaginal ulceration had 0.01 mgm/100 ml. blood ascorbic acid level; 150 mgm. three times a day for three days and 100 mgm. three times a day for one month prescribed. Controlled in five days. Lawlor and Richardson, *Brit. M. J.*, I. 254 (Feb.) 1914.

Wound Healing: 1 gm. a day for three days in vitamin C deficient patients and 100 mgm a day maintained saturation. Hunt, *Brit. J. Surg.*, 28: 436 (Jan.) 1941, through *Am. J. Dis Child*, 63: 621 (Mar.) 1942. Fasting ascorbic acid level of less than 0.2 mgm/100 ml. must be reached before there is produced a decreased ascorbic acid content and tensile strength in healing wounds in skin and fascia. Bartlett, Jones, and Ryan, *New England J. Med.*, 226 474 (Mar.) 1942.

Lactational Mastitis. Given orally, 50 mgm. daily to 121 pregnant women: 26.7% developed suppurative and 3.3% nonsuppurative mastitis. Incidences in the control group of 126 were 23.6% and 7.3% respectively. Fulton, *Brit. M. J.*, II 488 (Oct.) 1915.

ASPIRIN

(Acetyl salicylic acid)

Mice—

Toxicity. 600 mgm/kg. caused convulsions in four of ten within 10 to 15 minutes, and 800 mgm/kg. caused convulsions in three of five and

death of two in 90 minutes. Woolfe and MacDonald, J. Pharmacol. & Exper. Therap., 80: 300 (Mar.) 1944.

Rats—

Metabolic Products: 2,5-dihydroxybenzoic acid (gentisic acid) was thought to be increased after aspirin or methyl salicylate administration. Test given. Lutwak-Mann, Biochem. J., 37: 246 (July) 1943.

Man—

Overdosage: 65 gm. orally. Treated with large intravenous doses of sodium bicarbonate, glucose, saline and plasma and intramuscular cortical adrenal extract caused recovery. (6,600 ml. 5% glucose in 0.2 N saline containing 41 gm. sodium bicarbonate + 500 ml. plasma plus 8 ml. cortical adrenal extract). Oakley and Donnell, Brit. M. J., I: 787 (June) 1942.

Toxicity: 10–30 gm. reported to be the lethal dose. One death in 752 attempted suicides; dose range: 5–95 gm. Editorial, New Orleans M. & S. J., 98: 179 (Oct.) 1945.

Poisoning: 50 gm. orally caused onset of severe toxic symptoms 14 hours later; rapid respiration (40 per minute), strongly acid urine, mild pyrexia, disorientation and drowsiness and toxic hepatitis. Recovery followed gastric lavage with sodium bicarbonate, administered with large amounts of fluids and 2 gm. sodium bicarbonate every two hours, insulin and glucose started on second day plus a high carbohydrate diet. Charters, Brit. M. J., I: 10 (Jan.) 1944.

Poisoning: 81 gm. caused profuse sweating, increased pulse, vomiting, and finally stupor, delirium and visual auditory hallucinations. Gastric lavage and intravenous use of 500 ml. normal glucose-saline caused recovery. Hopkins, Lancet, 248: 145 (Feb.) 1945.

Deaths: 24 tablets containing aspirin and phenacetin. Chemist and Druggist, 143: 449 (May) 1945. *Suicide* with 100 tablets aspirin, Ibid., 143: 412 (Apr.) 1945. 4 doses 0.17 gm. at four hour intervals to four months old infant increased respiration, induced convulsion, death. Hemorrhagic complication at autopsy. Ashworth and McKemie, J.A. M.A., 126: 806; 1944.

Tonsillar Hemorrhage: Occurred in only four (1.4%) of 283, given postoperatively three or four rectal suppositories, each containing 0.6 gm. aspirin, 0.015–0.03 gm. codeine phosphate and 10 mgm. Synkayvite [tetrasodium salt of 2-methyl-1,4-naphthohydroquinone diphosphoric acid ester] or two tablets containing 0.3 gm. aspirin and 5 mgm. Synkayvite. Neivert, Arch. Otolaryng., 42: 14 (July) 1945.

Allergy: 0.6 gm. caused severe reaction with facial swelling, dyspnea, dysphonia, dysphagia, rapid irregular pulse, in 62 year old, two hours after taking. Responded to adrenaline 1 ml. and hot applications. Neill, Brit. M. J., II: 876 (Dec. 30) 1944.

Metabolic Products: 1.2 gm., oral, gave positive test 7-15 hours with urine. Lutwak-Mann, Biochem. J., 37. 246 (July) 1943.

ATROPINE

Rats and Mice—

Denervated Skeletal Muscles did not lose weight with 5 and 10 mgm. per 100 gm. 15 mgm/100 gm. caused weight loss. Doses were given subcutaneously in 1% solution for two weeks. Fischer, Proc. Soc. Exper. Biol. & Med., 51: 208 (Nov.) 1942.

Man—

Primary Dysmenorrhea: 0.65 mgm. three times daily beginning two days before expected period relieved 50 of 53 patients. Disagreeable side effects. Branscomb, J.M.A. Alabama, 12 81 (Sept) 1912.

"T" Waves: 1.33 mgm given subcutaneously lowered "T" waves in five, and in one subject resulted in development of A-V node rhythm changing to sinus tachycardia in twenty minutes. Hartwell et al., J. Clin. Investigation, 21. 409 (July) 1912.

ATROPINE SULFATE

Dogs—

Experimental Coronary Occlusion 0.1 mgm/kg five minutes after occlusion reduced mortality rate in conscious dogs to 50% and in anesthetized dogs to 34%. LeRoy, Fenn, and Gilbert, Am Heart J., 23: 637 (May) 1912.

Man—

Gastric Ulcer Treatment Intravenously, 0.33-0.66 mgm. as 1:1,000 solution of sulfate for 10 or 20 successive days. Reduced iron given three times daily, 0.1-0.2 gm. This healed the peptic ulcer more rapidly than protein treatment, amino acid or any other treatment. Henszelmann, Wien. med. Wchnschr., 91 681 (Aug) 1911, through J.A.M.A., 119: 531; 1912.

Parkinson's Disease 0.7% solution three times daily was gradually increased in accordance with tolerance and need. Most cases maintained on 5-10 mgm. three times day. Doshay and Ford, New York State J. Med., 42. 1060 (June) 1912. 18 mgm. as 0.5% solution three times a day, grad-

ually increased until maximum amount that could be tolerated with most benefit was reached with least toxicity. Bohn, Harper Hosp. Bull. (Detroit, Mich.), 1: 136 (June) 1942.

Pulmonary Embolism Therapy: Patient put in semi-sitting position and given oxygen inhalation plus 0.87 mgm. of atropine hypodermically. If there was no resultant flushing of face and dilatation of pupil, 1.0-0.87 mgm. atropine sulfate intravenously, also 32 mgm. papaverine hydrochloride intravenously were given. Both drugs were repeated every three to four hours until there was definite improvement and then three to four times a day. Johnson, Illinois M. J., 85: 13 (Jan.) 1944.

AVIDIN (Egg White)

Man—

50% Tumor Reduction (squamous cell carcinoma, tongue) 32-42 egg whites per day for 315 days. (Similar effects in other cancers.) Kaplan, Am. J. M. Sc., 207: 733 (June) 1944.

BACITRACIN

Mice—

Protection: Intraperitoneal injection of one or two units immediately following injection of 10,000 M.L.D. hemolytic streptococci protected 80% from infection. Johnson, Anker, and Meleney, Science, 102: 376 (Oct.) 1945.

Guinea Pigs—

Protection: Injection of 50-100 units plus a lethal dose of clostridial organisms followed by 50-100 units every three hours for 36 hours prevented development of gas gangrene. Ibid.

BACTERIOPHAGE

Man—

Bacillary Dysentery: Case mortality has fallen from 25% to 5% since use of anti-dysentery bacteriophage. 2 ml. ampoule, given as soon as diagnosis was established, was followed by one ampoule every four hours. Compton, Brit. M. J., 1: 719 (June) 1942.

BARBITAL SODIUM

Dogs—

Drug Fixation: 250 mgm/kg. given intravenously to five dogs were united after two hours with etherized dogs by cross circulation for one

hour. Recovery from barbiturate occurred in 27 minutes in cross circulation dogs and 29 hours in six control dogs. Koppányi and Linegar, *Science*, 96, 562 (Dec.) 1942.

Hunger Contractions. 100–150 mgm/kg. caused immediate and complete abolition of gastric hunger contractions in fasting animals but did not antagonize hypermotility from 15 units insulin given intravenously. 250 mgm/kg. suppressed posthypoglycemia exaggeration of stomach movements. La Barre and Vesselovsky, *Arch. internat. de pharmacodyn. et de therap.*, 66: 414 (Nov.) 1941.

Man—

Barbiturism Therapy. If not more than ten hours duration, cleansing of stomach plus apomorphine should be tried; intramuscular injection up to 6–7 mgm adrenaline per 24 hours or ouabain intravenously; caffeine or camphor subcutaneously were also given. Savy, *Union méd. du Canada*, 72 1428 (Dec.) 1943

Withdrawal Convulsions 50 mental patients without epilepsy taking 1.3 to 2.0 gm. in aqueous solution daily for one and one-half years or more, when deprived of drug, developed generalized convulsions in four to five days. Kalinowsky, *Arch. Neurol. & Psychiat.*, 48, 916 (Dec.) 1942.

BARBITURATES

Rats—

Detoxification: Intraperitoneally, 25–200 mgm/kg after post-operation fast following partial hepatectomy, others were completely nephrectomized after 24 hours of fasting, and then injected intraperitoneally with 30–200 mgm/kg. Indices of hepatic and renal detoxification for 29 barbiturates were given. The liver and kidney were the main sites of detoxification; deprivation of either organ did not prevent recovery. Nephrectomized animals always recovered. Masson and Beland, *Anesthesiology*, 6: 483 (Sept.) 1945.

Dogs—

Tolerance: Duration of anesthesia decreased markedly with daily administration intravenously of 30 mgm. evipal sodium per kg., 20 mgm. pentothal sodium per kg. or 30 mgm. Nostal sodium per kg. Tolerance was temporary. Tolerance to pentothal sodium lasted two weeks. Cross tolerance noted. Green and Koppányi, *Anesthesiology*, 5: 329 (July) 1914.

Man—

Action on Cerebral Cortex: Intravenous dose of 0.25–0.65 gm. amytal sodium, 0.3 gm. pentobarbital sodium, and 0.125–0.5 gm. pentothal sodium resulted in appearance of high voltage fast activity (21–32 cycles

per second) recorded on electroencephalogram. When a large amount was given, frequency slowed and delta waves of three to four per second appeared. The effects of barbiturates progress from frontal lobes through parietal to occipital region; recovery in reverse order. Brazier and Finesinger, *Arch. Neurol. & Psychiat.*, 53: 51 (Jan.) 1945.

Overdosage Therapy: Gastric lavage with 1:5,000 potassium permanganate solution, sodium sulfate or phosphate introduced by lavage tube; colon irrigation with 1:5,000 potassium permanganate followed by instillation of black coffee; freeing of airway; administration of oxygen; artificial respiration; 10% glucose in normal saline intravenously or 50 ml. of 50% sucrose; and picrotoxin 3 mgm. of 0.3% solution intravenously every 20 minutes until facial muscle twitch was established. Plasma indicated for oxygen deficiency. External heat, frequent changes of position and good nursing. Gardner, *Pennsylvania M. J.*, 47: 451 (Feb.) 1944.

BENADRYL

(N, N-dimethyl β -benzohydroxyethylamine-HCl)

Man—

Mènière's Disease: 150–300 mgm. per day relieved three patients within 24 hours. McElin and Horton, *Proc. Staff Meet., Mayo Clin.*, 20: 417; 1945.

Epileptic Attack: Intravenously, 60 mgm. in five minutes aborted the usual five hour attack at the two hour level. *Ibid.*

Toxic Reactions: Sleepiness, dizziness, dry mouth, and nervousness in ten of 74. Other reactions were urinary frequency, fatigue, epigastric distress, difficulty in coordination, nausea, bleeding tendency, sense of relaxation, diarrhea, constipation, excessive perspiration, tinnitus, and blurring of vision. Generalized pruritis developed in one patient after intravenous administration. *Ibid.*

Methods of Administration: Orally, 50–500 mgm. per day; intramuscularly in 20 mgm. injections, and intravenously, 10–120 mgm. within ten minutes by continuous drip. *Ibid.*

Urticaria Therapy: Orally, 50–100 mgm. from two to five times a day relieved 34 and improved 12 of 50 patients. O'Leary and Farber, *Proc. Staff Meet., Mayo Clin.*, 20: 429; 1945.

Bronchial Asthma and Hay Fever: Orally, 50–100 mgm. three times daily benefited 57 of 83 patients. Koelsche, Prickman, and Carryer, *Proc. Staff Meet., Mayo Clin.*, 20: 432; 1945.

Head Allergy: Half hour after 50 mgm. was given, relief was evident in perennial vasomotor rhinitis, myalgia, Ménière's disease, and vasodilat-

ing pain and lasted for two hours. 300 mgm. in six divided doses at two hour intervals maintained patients asymptomatic. Williams, Proc. Staff Meet., Mayo Clin., 20: 434, 1915.

Allergy in Children. 4.1 mgm/kg. per day given in two to four doses was suggested for treating hay fever, asthma, vasomotor rhinitis, urticaria, and serum reaction. Logan, Proc. Staff Meet., Mayo Clin., 20: 436; 1915.

BENZENE

Rats and Dogs—

Chronic Toxicity. Exposure to 1,000 p.p.m. seven hours daily, five days a week, for 28 weeks. A relative lymphopenia was followed by leukocytosis and lymphocytosis. Differential indicated changes in neutrophils and lymphocytes only. Svirbely, Dunn and von Oettingen, J. Indust. Hyg. & Toxicol., 26: 37 (Feb.) 1944.

Man—

Acute Poisoning: Depression of central nervous system.

Chronic Poisoning Damage of circulatory system. Maximum allowable concentration is 0.32 mgm./liter of air at 25°C. 760 mm. Hg for exposure of not more than eight hours. Benzene anemia treated with vitamin C, liver and iron. Natl. Institute of Health, Div. of Indust. Hyg., Pub. Health Rep., 56: 519 (Mar. 14) 1941.

BENZESTROL

Rats—

Effects: Oral and parenteral, three micrograms to three mgm. per week produced same effect on formed elements of blood and bone marrow as natural estrogen. Stebbins and Blanchard, Endocrinology, 36: 305 (May) 1915.

BENZOIC ACID

Rats (White)—

Toxicity: LD₅₀, intravenously as sodium salt, 1714 ± 0.121 gm/kg. Hager, Chapman, and Statkev, J. Am. Pharm. A (Scient. Ed.), 31: 253; 1912.

BENZOXAZOLES

Mice—

Anticonvulsant 0.3 gm/kg. of 2-benzylbenzoxazole, most active of 11 compounds prepared, elevated the convulsive threshold to more than 50 milliamperes and had an LD₅₀ of 1.75 gm/kg., 2-n-heptylbenzoxazole (LD₅₀, 2.3 gm/kg.) and benzimidazole in doses of 0.38 and 0.17 gm/kg., respectively caused a similar elevation. 100% death with 0.1 gm/kg. of

2-methyl-benzoxazole resulted in 24 hours. Bywater et al., J. Am. Chem. Soc., 67: 905 (June) 1945.

BENZYL ALCOHOL

Man—

Fatal (Mother and Child): Six ml. as vehicle for 12 ml. paraldehyde rectally (obstetric analgesia). Speert, J.A.M.A., 118: 66; 1912; also Shoor, J.A.M.A., 117: 1534; 1941 reported as paraldehyde death.

BENZYL BENZOATE

Dogs—

Demodectic mange: Local application of 33% aqueous solution containing 51% alcohol (Zylate) every third day for two to three treatments gave quick response without toxic reactions or skin irritation. Davidson, Vet. Med., 40: 377 (Nov.) 1945.

Man—

Ptyalism in Pregnancy: Three doses of 20 drops, 25% solution in 90% alcohol, given in water every two hours and then every four hours. Dramatic response. Nelson, Brit. M. J., II: 414 (Sept.) 1945.

Pruritis Ani: Local application of 25% solution three times per day. Russo, Virginia M. Monthly, 72: 394 (Sept.) 1945.

Scabies: 20% emulsion satisfactory in treatment. Mellanby, Johnson, and Bartley, Brit. M. J., II: 1; 1942 (see sulfur). One single application of emulsion over whole body of inmates in institution reduced incidence almost to nil. Mellanby, Brit. M. J., I: 689; 1944.

BILE SALTS

Mice—

Threshold Cathartic Dose: 40 mgm. per mouse. 20 mgm. daily induced no active catharsis. No tolerance developed with daily sub-threshold doses for 150 days. Hazleton and Fortunato, J. Am. Pharm. A. (Scient. Ed.), 31: 60; 1942.

BIOTIN

Chicks—

Requirement: 7–10 micrograms per 100 gm. of ration. Hegsted et al., J. Nutrition, 23: 175; 1942.

Domestic Fowl—

Reproduction: Lack of biotin reduced hatchability from 80% to less than 20% in six weeks. 15 micrograms concentrate per 100 gm. ration

remedied (to former 80%) in three weeks. Cravens et al., *Proc. Soc. Exper. Biol. & Med.*, 50: 101 (May) 1942.

Rats—

Leukopenia and Subnormal Growth from sulfasuxidine feeding overcome by 0.5 gamma biotin daily and either folic acid concentrate or liver extract with as much folic acid as 0.1 gm. of standard. Ransone and Elvehjem, *J. Biol. Chem.*, 151: 109 (Nov.) 1913.

Procarcinogenic Effect. 0.3-4.0 gamma crystalline biotin daily effective when butter yellow was fed in highly protective diet. Vigneaud et al., *Science*, 95: 174 (Feb.) 1942.

Dogs—

Paralysis: Subcutaneously, 100 micrograms per kg. cleared five of seven of progressive paralysis due to vitamin B complex deficient diets Smith, *Am. J. Physiol.*, 144: 175 (July) 1945.

Man—

Cure of "Egg White Injury": Minimum daily dose of 150 gamma for prompt relief. Sydenstricker et al., *Science*, 95: 176 (Feb. 13) 1942. 150-300 micrograms concentrate daily gave relief in three to five days. Sydenstricker et al., *J. A. M. A.*, 118: 1199, 1942.

BISMUTH

Man—

Stomatitis and Albuminuria developed from 0.2 gm. bismuth subsalicylate injected intramuscularly every week. It should be administered with caution in those with a tendency toward acidosis, diabetes, renal damage, intercurrent infections, impaired food intake or absorption and cardiac disease. Peters *Am. J. Syph., Gonorr., & Ven. Dis.*, 26: 81 (Jan.) 1942.

Threadworm Therapy in Children. Bismuth meal of 30-60 gm. for a five-year-old, larger dose for older children (barium meal also effective in many cases). Repeated in three weeks because of three-week cycle in development of threadworms Lapage, *Brit. M. J.*, 1: 738 (June) 1912.

BISMUTH ARSPHENAMINE SULFONATE

(Bismarsen)

Man—

Lupus Erythematosus Intramuscular injection of 0.05 gm. twice weekly for one week to test tolerance, then 0.1 gm. twice weekly sometimes raised to 0.2 gm. twice weekly. Recovery in 50%. 12 of 28 showed improvement, two, no improvement Weiss et al., *Arch. Dermat. & Syph.*, 44: 1009 (Dec.) 1911.

BISMUTH ETHYL CAMPHORATE**Man—**

Early Syphilis: Intramuscular injection of two ml. (40 mgm. bismuth per ml.) at weekly intervals for 10–12 doses. *S. pallida* disappeared in two to seven days. Alexander and Schoch, Arch. Dermat. & Syph., 45: 876 (May) 1942.

BISMUTH SODIUM TARTRATE**Man—**

Arthritis: Intramuscularly, 0.03 gm. in a stable solution given at four week intervals, and then at less frequent intervals of six weeks, two or three months. Hall, Lancet, 249: 385; 1945. One ml. of 3% solution dissolved in isotonic glucose and preserved with 0.5% phenol (strength 0.06 gm./ml.) injected deeply into gluteal muscle caused slight reaction. Second dose was not given before lapse of two weeks, and period was soon extended to three to four weeks or more. Hall, Lancet, 246: 264 (Feb.) 1944.

Syphilis Therapy: 1–2 ml. 3% aqueous bismuth sodium tartrate given intravenously, weekly and twice weekly were well tolerated. Neoarsphenamine or maplarsen was given in alternate series. Reaction: temporary aching of jaws and teeth, anorexia, skin reaction, salivation, occasional nausea and vomiting; no renal damage. Hudgins, M. Times, 72: 156 (June) 1944.

BISMUTH SUBNITRATE**Man—**

Methemoglobinemia: 12 gm. (two gm. per six hours) produced dyspnea and cyanosis in a diabetic. Recovery with oxygen solarium and whole blood transfusion. Miller, Gastro-enterol. 4: 430 (May) 1945.

BISMUTH SUBSALICYLATE**Man—**

Linear Scleroderma: 12 intramuscular injections of 0.8 gm. caused 75% improvement in disease of nine years' duration. Anderson, Arch. Dermat. & Syph., 45: 1217 (June) 1942.

BLOOD**Dogs—**

Shock: 62.5% dogs in "irreversal" stage of shock survived with whole blood supplemented by sodium bicarbonate and glucose. Blood plus other substances gave the following survival rates in each group of eight: sodium succinate (0.42 gm. of anhydrous salt/kg.) 50%; sodium lactate (0.58 gm/kg.) 75%; glucose (0.38 gm/kg.) 37.5%; sodium bicarbonate

BORIC ACID

Experimental Animals—

Median LD: Intravenous, oral, and subcutaneous doses varied between 1.2 to 3.45 gm/kg. The intravenous route was most toxic and guinea pigs were most susceptible. Pfeiffer, Hallman, and Gersh, J.A.M.A., 128: 266; 1945.

Dogs—

Acute Toxicity: Orally, two gm/kg. was lethal to three of six; subcutaneously, one gm/kg. was lethal to two of four. Ibid.

Cumulative Effect: After therapy with 10% ointment for 25 days, content of brain was 212 mgm., liver 107 mgm., body fat 30 mgm. Absorption: Toxic quantity was absorbed by irrigation of abdominal cavity for three hours with 5% boric acid. Ibid.

Excretion: 60% of amount ingested was excreted in 48 hours. 50–400 mgm. injected intravenously produced sharp rise in excretion and a gradual rise in phosphorus excretion which greatly exceeded control values six hours later. Ibid.

Infant (4.5 months old)—

Skin Absorption: 60–100 gm. applied topically in ointment on three occasions resulted in convulsive seizures, intense erythema, deafness, and death. Watson, J.A.M.A., 129: 332; 1945.

BORON

Rats—

Requirement: 0.6 microgram per rat per day, if boron is needed for normal growth. Teresi et al., Am. J. Physiol., 140: 513 (Jan.) 1944.

BOTROPASE

(Venom of *Botrops jararaca*)

Pigeons—

Hemocoagulative Activity occurred in dose equivalent to 0.0002 mgm. of venom which was $\frac{1}{6000}$ of toxic dose. Vaz and Pereira, São Lucas Medical Soc. Meeting, through J.A.M.A., 116: 2521; 1941.

Man—

Hemorrhage: Intravenous injection of one ml. for immediate effect followed by one ml. subcutaneously if there was danger of bleeding. *Prophylaxis:* Subcutaneous or intramuscular dose of one ml. given two to three hours before surgery. Ibid.

BROMIDES

Man—

Delirium: 350 mgm.% serum bromide level caused delirium. Disappeared in ten days after drug was withdrawn. Levin, J. Nerv. & Ment. Dis., 102: 256 (Sept.) 1945.

Intoxication: <100 mgm.% in blood caused intoxication characterized by dull headache, constipation, fatigue, irritability, restlessness, anorexia, lack of concentration and poor memory. 250 mgm.% blood level caused mydriasis, diminished knee jerks, furred tongue, foul breath, tremulous speech, marked confusion and disorientation, frightening hallucinations, weight loss, and cachexia. Kay, Smith, and Johnson, J. M. A. Alabama, 13: 284 (Mar) 1944.

Blood/Spinal Fluid Barrier: Intracisternally, sodium salt, in amounts too small to alter serum bromide level, lowered barrier to passage of bromide ion into spinal fluid Weir, Am J Physiol, 143: 83; 1945.

Bromide Intoxication Symptoms, in decreasing order: mental confusion, stupor, delusions, headaches, hallucinations, nervousness, weakness, gait disturbances, coated tongue, palpitation, slurred speech, etc. 150 mgm.% bromide blood level caused little or no symptoms in healthy, and as little as 75 mgm.% caused severe intoxication in those with malnutrition, arteriosclerosis, or anemia. *Treatment.* Six to eight gm. sodium chloride orally or parenterally and forced fluids. Sensenbach, J.A.M.A., 125: 769, 1944.

Blood levels of 300 and 500 mgm/100 ml. from prolonged use of headache powder containing 0.5 gm. potassium bromide, 0.15 gm. acetanilide. *Therapy:* Intravenous saline, fluid orally, 0.32 gm. sodium chloride orally every three hours for five days, then 0.65 gm. every two hours. Kraske and Platt, Ibid, 125: 107, 1944

Blood levels 130-450 mgm %. *Treatment* Intravenous sodium chloride to comatose. Others oral 0.66 gm three times daily or 2 gm three times daily or four times daily. Fall in blood bromide level averages 18.9 mgm/day, time required to clear symptoms 12-40 days. Five mgm. desoxycorticosterone acetate plus sodium chloride reduced time required for 50% reduction in blood bromide level from 8.5-14.5 days to four to eight days. Wohl and Robertson, Pennsylvania M. J., 47: 802 (May) 1911.

Bromide Intoxication Therapy If serum bromide was over 150 mgm.: sodium chloride six to ten gm. was given daily, also five ml. adrenal cortex extract per day for six to seven days or 10 gm. sodium chloride oral, five ml. adrenal cortex at 1.2 ml daily Boudurant and Campbell, J.A.M.A., 116: 100; 1911.

1,3 BUTADIENE

Rats (albino), Guinea Pigs, Rabbits, and Dogs—

Toxicity: 68% of 164 animals showed slight growth retardation and light cloudy swelling in livers at 6,700 parts per million butadiene; no progressive injury was found in concentration of 600, 2,300, and 6,700 parts per million. Exposure lasted eight months (six days a week, at 7.5 hours per day). No other changes noted. Carpenter et al., J. Indust. Hyg. & Toxicol., 26: 69 (Mar.) 1944.

Man—

Hippuric Acid Excretion: Increased seven gm. in 24 hours with exposure to 800 parts per million toluol for eight hours, and 3.2 gm. with exposure for four hours to 800 parts per million styrene. Ibid.

Psychomotor Response: Two exposed for four to eight hour periods to butadiene, toluol, and styrene. Styrene was most objectionable at 800 parts per million; toluol at 800, 600, 400, and 200 parts per million less objectionable; and butadiene at 8,000 parts per million had effect no greater than 200 parts per million toluol. Low concentration of toluol and butadiene had no effect on steadiness, and high concentration caused marked unsteadiness. Ibid.

n-BUTYL CHLORIDE

(1-chloro-butane)

Dogs—

Trichuriasis Therapy: 30 gm. intracecally for eight kg. dog. Single dose. Steinbach, Vet. Med., 37: 184; 1942.

BUTYN

(Dibutylaminopropyl-p-amino-benzoate sulfate)

Guinea Pigs—

Detoxication of convulsant toxic effects. See procaine.

Man—

Oral Surgery: Butyn, 0.75% compared with 2% procaine in 231 cases. Butyn anesthesia lasted one hour longer; caused pain on injection four times as often as procaine and had tendency to cause perspiration, nervousness, and occurrence of fainting greater. Procaine was drug of choice. Tainter, Thronsdon, J. A. Dent. A., 28: 1979 (Dec.) 1941.

CADMIUM

Man—

Poisoning: In 25 minutes after taking lemonade from cadmium-plated pitcher. (12 men.) Gastric lavage with sodium bicarbonate, water and sodium chloride orally, bismuth and paregoric orally, morphine hypodermically. Recovery in five hours. Lufkin and Hodges, U. S. N. M. Bull., 43: 1273 (Dec.) 1911.

Poisoning Symptoms: Nausea, vomiting, abdominal cramps and diarrhea, resulting in prostration and weakness. Cadmium probably combined with hydrochloric acid of gastric juice to form cadmium chloride which was irritating to nerve endings of gastric mucosa. U. S. Naval M. Bull., 43: 398 (Aug.) 1914.

Poisoning: Symptoms given. Therapy: rest in bed, oxygen therapy for dyspnea, sulfonamides for pneumonia and sedation for dry cough and gastric reactions. 23 cases with no fatality. Ross, Brit. M. J., I: 252 (Feb.) 1914.

CADMIUM CHLORIDE AND "AEROSOL" OT

Man—

Ringworm Therapy: Local application of 1% cadmium chloride and 1% "Aerosol" OT (sodium di-(2-ethylhexyl) sulfosuccinate) in 30% ethyl alcohol to lesions of scalp, forearms, and feet was effective. Coca, J. Lab. & Clin. Med., 29: 689 (July) 1911.

CADMIUM SULFIDE

Man—

Tuberculosis Therapy: 0.01 gm. suspended in oil injected once or twice weekly. No reactions or cumulative effects. Higher number of totally arrested and improved cases than after gold therapy. Ray, Sen and Das Gupta, Indian M. Gaz., 76: 203; 1911.

CAFFEINE

Color Test: A specified amount of an oxidizing mixture was added to 0.1 ml. of a caffeine solution in the presence of hydrochloric acid, evaporated on a low-temperature hot plate and heated to bring out maximum color. 0.05 ml. of triethanolamine solution was added to develop a final color. Morgan & Opolonick, Indust. & Engin. Chem. (Anal. Ed.), 17: 526 (Aug.) 1915.

Rats—

Gastric Ulcers: By stomach tube 75 mgm/kg body weight over a

period of 8-20 weeks caused alterations in the stomach that might be regarded as erosions or ulcers in only three of 34 rats. Giddings, Wynn, and Haldi, *Gastroenterology*, 5: 210 (Sept.) 1945.

Cats—

Effect: Intravenously, 0.21 gm. doses effected complete decurarization in the neuromuscular preparation. Huidobro and Amenbar, *J. Pharmacol. & Exper. Therap.*, 84: 82 (May) 1945.

Gastric Ulcers: By stomach tube, 75 mgm/kg. daily given for 21 days did not produce erosions or ulcers in the stomach. *Ibid.*

Man—

Pepsin Secretion: Orally, 500 mgm. or 0.1-0.2 mgm. histamine subcutaneously increased by approximately same degree the pepsin output of five young adults. More sustained response with caffeine. Simultaneous administration of caffeine and histamine produced a greater pepsin secretion during periods over 70 minutes than sum of response of two drugs administered separately. Grossman, Roth, and Ivy, *Gastroenterology*, 4: 251 (Mar.) 1945.

CAFFEINE SODIUM BENZOATE

Fatigue lessened by intravenous use of 0.5-1.0 gm. between work periods. Foltz, Ivy, and Barbarka, *Am. J. Physiol.*, 136: 79 (Mar.) 1942.

CALCIUM

Pullets—

Egg Shell Quality: 3.0% calcium in basal diet containing vitamin D and 0.8-1.0% phosphorus produced thicker egg shell than those receiving higher or lower calcium. Evans, Carver, and Brant, *Poultry Science*, 23: 36 (Jan.) 1944.

Dogs—

Death from Parenteral Calcium. 8.4% solution calcium in distilled water, injected at the rate of 4 ml. per minute into femoral vein. In normal animal 540 ml.; in parathyroidectomized animal, 496 ml. fatal. Bedinger et al., *J. Pharmacol. & Exper. Therap.*, 74: 1; 1942.

Monkeys—

Chronic Deficiency: 10.2 mgm. calcium per 100 gm. diet (190 mgm. calcium per 100 gm. in controls) led after one year to calcium depletion symptoms. Loss of weight, weakness, muscular atrophy, irritability, decreased activity and paralysis of the hind legs.

Calcium Plus Vitamin C Deficiency: Led to additive rather than synergistic effects. Fraser, *Publ. Health Reps.*, 57: 959 (June) 1942. Also *Ibid.*, 57: 968 (June) 1942. Pathology, Tomlinson, *Ibid.*, 57: 987 (July) 1942.

Man—

Maintenance Requirement for Men: 9.55 ± 0.46 mgm. per kg. body weight daily, when $\frac{2}{3}$ of calcium obtained from milk products. Steggerda and Mitchell, *J. Nutrition*, 21: 577 (June) 1941.

Requirement for Adults: 662 mgm. daily or 10.7 mgm/kg.: 3.9 mgm. per cm. height; 391 mgm./sq.m. surface area 752 mgm. calcium on 70 kg. weight basis. Outhouse et al., *J. Nutrition*, 21: 565 (June) 1941.

Hyperthyroidism. Two gm. daily was required to maintain calcium retention, three gm. daily if calcium content has been depleted. Daily loss—459 mgm. in patients maintained on a 474 mgm. daily intake for 90 days; 362 mgm. on an oral or parenteral intake of 2410 mgm. daily. Effective retention—high calcium and phosphorus diet supplemented daily with oral calcium gluconate 10 gm., calcium lactate 3 gm., 0.6 ml. Crystalline vitamin D in propylene glycol and intravenous administration of 10 ml. of 10% calcium chloride solution three times daily, or oral administration of dicalcium phosphate with viosterol. Puppel et al., *Surg. Gynec. & Obst.*, 81: 243 (Sept.) 1915.

CALCIUM CASEINATE

Man—

Peptic Ulcer Therapy. Antacid tablets containing 1.6 gm. calcium caseinate and 0.4 gm. calcium carbonate resulted in complete and continued relief of peptic ulcer symptoms in 87% of 40 patients, 90% and 10% of whom had duodenal ulcers and gastric ulcers respectively. Dose: one or two tablets every two hours and glass of milk on alternate hours for three months. March, *Jackson Clinic Bull.*, 6: 38 (Mar.) 1914.

CALCIUM CHLORIDE

Cows—

Stimulation of Uterine Contraction. Intravenously 50–250 ml. 20% calcium chloride and 50% glucose in physiologic saline Smith, *J. Am. Vet. M. A.*, 100: 232; 1912.

Man—

Hemorrhage: 0.65 gm. calcium chloride in water must be administered intramuscularly rather than orally. Grove, *Brit. M. J.*, 11: 727 (Dec.) 1913.

CALCIUM GALACTOGLUCONATE AND CALCIUM BROMIDE

Man—

Adjunct to Neurodermatitis Disseminata: Intramuscularly, 10 ml. solution containing 1.24 gm. active compound three times weekly plus one to three gm. effervescent tablets daily reduced itching in 20 patients. Reuter, Arch. Dermat. & Syph., 46: 881 (Dec.) 1942.

CALCIUM GLUCONATE

Man—

Edema: Generalized, after one gm. intravenously per day over six weeks. J.A.M.A., 125: 526 (June 17) 1944.

Malaria: Chills relieved by 10 ml. of 10% solution given slowly. Average length of chill reduced from 73.5 to 7.2 minutes (48 of 50). Relief in six cases in 15–50 seconds. By effects: headache, nausea, vomiting, epigastric discomfort, flushing of face, chest oppression, and dizziness. Stevenson, Porto Rico J. Pub. Health & Trop. Med., 19: 602 (June) 1944.

Wrist Fracture Therapy: (child): 2.0 gm. three times daily, (adult): 4 gm. plus 0.6–1.3 ml. hydrochloric acid in water before meals. Hoshall, J. South Carolina M. A., 38: 57 (Mar.) 1942.

Circulation Time: 5 ml. 20% calcium gluconate or 10% calcium chloride. Calcium is palatable, cheap, and useful. Winternitz, Lancet, 246: 295 (Feb.) 1944.

Tropical Ulcer: Intramuscularly, 0.5 gm. calcium gluconate or 0.50–0.1 gm. calcium chloride intravenously daily, effective. Charters, Tr. Roy. Soc. Trop. Med. & Hyg., 37: 205 (Dec.) 1943.

Tsutsugamushi: Intramuscularly, 10 or 20 ml. 10% solution daily or intravenously during acute pyrexial stage, average total dose was 99 ml., maximum total dose 140 ml. Sangster and Kay, M. J. Australia, 32: 138 (Aug.) 1945.

Infants—

Fatality. Intramuscularly, 10 ml. 10% solution for convulsions caused a fatality. Abscess formation at injection site. Lamm, J.A.M.A., 129: 347; 1945.

CALCIUM PANTOTHENATE

Man—

Glossitis: Orally, 150 mgm. daily effective within two to three weeks; 300 mgm. orally daily may be required.

Glossitis and Cheilosis: Intramuscularly, 100 mgm. three times daily, effective. Field, Green, and Wilkinson, Am. J. Digest Dis. & Nutrition, 12: 246 (July) 1945.

CALCIUM PHOSPHATE**Man—**

Spinal Osteoporosis: 1 gm and 5,000–10,000 International Units of vitamin D daily were tolerated and had therapeutic benefit. Other calcium salts were used. 1–4 gm. calcium salt and 3,000–30,000 units vitamin D daily relieved pain and caused clinical improvement in 20. Burrows and Graham, *Quart. J. Med.*, 14: 147 (July) 1945.

CARBARSONE

(N-carbamyl-arsanilic acid)

Man—

Amebiasis Therapy. 0.25 gm orally, twice a day for ten days effective. Lewis and Low, *Northwest Med.*, 41: 52 (Feb.) 1942.

Tropical Eosinophilia. Orally, 0.25 gm. twice daily in two to ten day courses, interrupted by ten day rest period. Emerson, *U. S. Nav. M. Bull.*, 42: 118 (Jan.) 1944.

CARBON DIOXIDE**Children—**

Infantile Paralysis: Inhalation, 5% mixture in oxygen for 24 to 36 hours, continuously, or for one to two hours daily caused prompt relaxation and relief of pain in 12 of 13. *Science News Letter*, 48: 227 (Oct.) 1945.

Man—

Altitude Tolerance. Carbon dioxide administration was only method of value for improving physiologic response to anoxia or relieving symptoms of anoxia for altitude of less than 13,000 meters. Also recommended—ammonium chloride plus high carbohydrate diet. Ruhl, *Deutsche med. Wchnschr.*, 69: 25 (Jan.) 1943, through *Bull. War Med.*, 4: 112 (Oct.) 1943.

Hyperventilation: Relief by administration of 5% carbon dioxide inhalation by rebreathing and by holding the breath. Kirk, *J. Oklahoma M. A.*, 37: 59 (Feb.) 1944.

CABON DISULFIDE**Dogs—**

Chronic Poisoning: In eight dogs, air contained 400 p p m. over eight hours, five days a week for 10–15 weeks, developed neurologic disorders.

Man—

Thiamine Excretion: Seven exposed to concentration of 5–25 p.p.m. for one or more years showed no thiamine deficiency as determined by urine assay (thiochrome method). Rubin, *Indust. Med.*, 13: 223 (Mar.) 1944.

Maximal Permissible Concentration: 20 parts per million parts of air by volume corresponding to 0.062 mgm/L. at 25°C. and 760 mm. Hg for exposures not exceeding a total of eight hours daily. Pub. Health Rep., 56: 574 (Mar.) 1941.

CARBON MONOXIDE

Safe Limits in Air: 100 p.p.m. Kehoe, *Illinois M. J.*, 85: 261 (May) 1944.

CARBON TETRACHLORIDE**Mice—**

Hepatoma: Administration of 32, 16, 8, 4, and 2% solutions in olive oil by stomach tube to 30 mice for total period of intermittent exposure of 29, 58, 87, 116, and 145 days respectively. The incidence of hepatoma increased with increase of total time during which the carbon tetrachloride was administered; i.e., size of dose and interval between doses were determining factors. Eschenbrenner and Miller, *J. Nat. Cancer Inst.*, 4: 385 (Feb.) 1944.

Rats—

Effect of Food on Poisoning: Administration of five doses of 4–5 gm. sucrose or glucose per kg. over 12 hours following carbon tetrachloride kept the liver neutral-fat content at normal level. Three equivalent doses over six hours permitted fatty infiltration of the liver, and a nearly similar result was obtained with five doses of 2 gm/kg. over 12 hours. Five doses of 3 gm/kg. at four hour intervals did not prevent a definite rise in neutral fat content in liver. Dillard, Spence, and Forbes, *Virginia M. Monthly*, 71: 154 (Mar.) 1944.

Exposure: 1,000 parts per million parts of vapor for six hours daily for 14 successive days caused no depletion of sulfur in liver tissues. Shaffer and Critchfield, *Proc. Soc. Exper. Biol. & Med.*, 59: 210 (June) 1945.

Dogs—

Effect of Food on Poisoning: 2 gm. sucrose/kg. every four hours for four days produced normal neutral fat content in liver. Amino acid 2 gm/kg. for five doses at three hour intervals produced no effect, but amino acids and carbohydrates combined gave good results. Dillard, Spence, and Forbes, *Virginia M. Monthly*, 71: 154 (Mar.) 1944.

Experimental Therapeutics

Hepatic Damage: 0.5 ml/kg. body weight twice tube in ten days, seven developed abnormal liver function. Of the liver function tests studied, the bromosulphonphthalein retention (5 mgm. dose) was most sensitive in detecting the type of damage produced. Drill and Ivy, J. Clin. Investigation, 23: 209 (Mar.) 1944.

Poisoning: Recovery with supportive therapy plus 6-12 gm. per day methionine by mouth or indwelling duodenal catheter. Eddy, Indust. Med., 14: 283 (Apr.) 1945. 30-40 ml. swallowed, resulted in hepatic dysfunction. Therapy with 0.1 gm. phenobarbital on day of poisoning and 2 gm. d,l-methionine, orally, 436 ml. casein digest and methionine solution intravenously by continuous infusion the second and third day. Recovered. Beattie et al., Brit. M. J., 1: 209 (Feb.) 1944. Nausea, abdominal pain, vomiting, weakness, cough, headaches occurred in workers in a parachute plant using carbon tetrachloride (Carbona). One became severely ill, had urine albumin and hyaline casts, calcium content was subnormal. Treatment consisted of adequate ventilation, rotation of workers, drinking one quart milk a day, and avoiding greasy foods, oily laxatives, and alcohol. Doyle and Baker, Indust. Med., 13: 184 et seq. (Feb.) 1944. All cases reported in literature during ten years from 1932 given in detail as to length of exposure, symptoms, length of illness. Quadland, Indust. Med., 12: 821, 1943.

Teniasis: Cured by 0.5-3.0 ml according to age of patient. Cure rate 80%. Toxicity. drowsiness and giddiness of short duration. Mukerji and Maplestone, Indian M. Gaz., 78: 282, 1913. Trop Dis Bull 40: 925 (Dec.) 1943.

CARBOXY-SULFATHIAZOLES

Mice—

LD₅₀: Intraperitoneally, 1.0-1.3 gm/kg of 4 thiazole derivative. Poth and Ross, J. Lab. & Clin. Med., 30: 843 (Oct.) 1915.

Dogs—

Bacteriostatic Activity. Orally, 1 gm of the 2-(p-aminophenyl-sulfonamido) derivatives of 4- and 5-thiazole carboxylic acid in six divided doses daily significantly altered the gastrointestinal coliform flora. Maximum blood concentrations and urinary concentration varied from 6-18 and from 335-2200 mgm per cent, respectively. Anticoliform activity of 4,5-thiazoledicarboxylic acid was intermediate between that of sulfasuxidine and sulfathalidine, the respective equivalent doses being 0.5, 1.0, and 0.25 gm/kg. Repeated administration intravenously of 1 gm/kg was well tolerated. Ibid.

CARNOSINE

Monkeys (intestine)—

1.5 mgm/100 ml. bath stimulated isolated intestine. Relaxation with morphine in 25 tests. Carnosine given previously, followed by a large dose morphine did not cause relaxation. Slaughter, Johnson, and Gales, *Proc. Soc. Exper. Biol. & Med.*, 48: 95 (Oct.) 1941.

CAROTENE

Chickens (Hens)—

Absorption and Retention: 16% absorbed on a low fat ration of 0.07% fat, and 67% on normal ration of 3.8–4.0% fat. Russell et al., *J. Nutrition*, 24: (Sept. 10) 1942.

Rats—

β -carotene Excretion: 12–14% excreted on diets containing 204–544 micrograms β -carotene per day. Ramasarma and Hakim, *Nature*, 149: 611 (May) 1942.

Influence of Vitamin E: One microgram in diet produced a 3.2 kg. gain in five weeks as compared to a gain of 7.6 kg. when 38.6 microgram α -tocopherol was included Rao, *Nature*, 156: 449 (Oct.) 1945.

Absorption: 350 micrograms/ml. in solution and total concentration of 3,750 micrograms/ml. in which 65% was in suspension. Rates of absorption in three hour tests were 9 and 100 micrograms per 100 sq. cm. per hour, respectively. Carotene concentration was maximum at 12 hours, considerable amount still remained in gut wall after 42 hours. Shaw and Deuel, *J. Nutrition*, 27: 395 (May) 1944.

Cows (Calves)—

Requirement: For maintenance of normal spinal fluid pressure in Holstein and Ayrshire calves was 66 micrograms carotene per kg. per day during the winter months. Moore, Berry, and Sykes, *J. Nutrition*, 26: 649 (Dec.) 1943.

Minimal Requirement: 127/0.5 kg. per day at environmental temperature of 50–70°F. <277/0.5 kg. per day were not fully protective under average winter conditions. Keener and Bechdel et al., *J. Dairy Sci.*, 25: 571 (July) 1942.

Cows—

Blood Plasma Content. Orally 5 mgm. daily increased level of 0.05–0.08 mgm.% to 0.76 mgm.% in 41 days. Orally 1000 mgm. daily in one cow increased level from 0.75–2.33 mgm.% in 54 days. Intrajugular injec-

tion of 400-900 mgm. caused no detectable change. Goss and Mead, J. Dairy Sci., 24: 521 (June) 1941.

Requirement in Lactation: 40 micrograms per 0.5 kg. daily. Kuhlman and Gallup, J. Dairy Sci., 24: 522 (June) 1941.

Man—

Urolithiasis Prevention: Carotene in oil or halibut liver oil six to eight capsules per day. Patients with positive reaction to night blindness 200,000-500,000 units in 24 hours. Stewart, Illinois M. J., 81: 402 (May) 1942.

CASEIN

Rats—

Hepatic Injury: 18% casein in diet prevented hepatic injury but 10% or less allowed necrosis and cirrhosis. Amount of casein was central factor in producing hepatic injury. Addition of choline to diet in which butter was a source of fat completely prevented liver injury. Gyorgy, Am. J. Clin. Path., 14: 67 (Feb) 1944.

Man—

Burns and Wounds. Casein solution which dried quickly and formed aqueous soluble non-contracting film proved effective. Autoclaved: 30 gm. casein, 4 gm. sodium lauryl sulfate, 10 ml. 50% sodium lactate, 0.7 gm. sodium hydroxide, and 140 ml. water to form a clear amber liquid, pH approximately 8, stable at ordinary temperature in tightly closed container. Curtis and Brewer, Arch. Surg., 48: 130 (Feb.) 1944.

CASHEW NUT OIL

Man—

Contact Dermatitis: Desensitization accomplished with five intramuscular doses of 0.5 ml. 2% solution of cashew nut oil extract every five days was followed by tolerance dose of 0.5 ml. given every five weeks for three doses. Lockey, Ann. Allergy, 2: 22 (Jan-Feb) 1944.

CELLULOSE ACETATE PHTHALATE

Rats—

Chronic Toxicity. 5, 20 or 30% in diets for one year caused no consistent pathologic changes except reduction in growth with large doses. Hodge, J. Pharmacol. & Exper. Therap., 80: 250 (Mar.) 1944.

Dogs—

Chronic Toxicity. 1, 4 or 16 gm. for one year showed very low order of toxicity. Ibid.

Man—

Enteric Coating: Barium sulfate tablets and enteric capsules given to man disintegrated mostly in four to six hours by radiographic study. Site of disintegration was the intestines. Hodge, Forsyth, and Ramsey, J. Pharmacol. & Exper. Therap., 80: 241 (Mar.) 1944.

CERBERIN**Man—**

Auricular Fibrillation: Controlled more rapidly than digitalis intravenously five cat units daily to ten patients; orally, in doses sufficient to slow the apex rate to the desired level and reduce the pulse deficit to a minimum. Bond, Baum, and Dimond, Am. Heart J., 30: 194 (Aug.) 1945.

CETILPYRIDINIUM CHLORIDE**Frogs—**

Action: Intracranially, 0.01 ml. of 1:100 solution at the juncture of cord and brain stem caused typical strychnine convulsions. Warren et al., J. Pharmacol. & Exper. Therap., 74: 401 (Apr.) 1942.

Rabbits—

Acute Toxicity: Intravenously, 20 mgm/kg.; $LD_{50} = 35$ mgm/kg. Oral, 400 mgm/kg. killed one of six. Intraperitoneally, most toxic.

Chronic Toxicity: Oral, 10 mgm. and 100 mgm/kg. daily for four weeks, had no significant harmful effect. *Action*, 15–20 mgm. intravenously caused paralysis which spread to abdomen and respiratory muscle. Ibid.

Dogs—

Action. Intravenously, 25–30 mgm/kg. caused curare-like action. Ibid.

Man—

Urolithiasis: Introduction into the kidneys of 2 ml. (of a 1:10,000 dilution during the first six months and 1:8,000 during the last six months), withdrawn by suction; followed by an additional 2–5 ml. which drained naturally for from five to ten minutes, and a final 5 ml. which was allowed to remain in the urinary tract, rendered the urine sterile in six of 14. Ezickson, J. Urol., 54: 235 (Sept.) 1945.

CH'ANG SHAN

(From roots of *Dichroa fibriga*, Lom)

Man—

Antimalarial: 0.03–0.06 gm. extract (equivalent to 7.5–15.0 gm. drug) orally two or three times daily for five days effective. Jang et al., Science, 103: 59 (Jan. 11) 1946.

Chicks infected with *Plasmodium gallinaceum* given 1 gm/kg. orally, twice a day for one to seven days. Ibid.

Acute Toxicity:

Dogs: LD₅₀. 20 gm/kg.; ducklings: 22 gm/kg.; chicks: 14 gm/kg. Ibid.

CHAULMOOGRA

Man--

Early Leprosy: Successful therapy, with large doses of ethyl esters of chaulmoogra, 30 ml. per week for seven to ten months. Smaller doses to intolerant patients. Basombrio, Rev. argent. dermatosif., 27: 238 (June) 1943.

CHINIOFON

Man--

Amebiasis: 1 gm., three times a day for eight to ten days or as a retention enema. When necessary to repeat course, a two week rest period was allowed. Major drawback was watery diarrhea. Flynn, J. Iowa M. Soc., 35: 360 (Sept.) 1945.

CHLORIDES

Man--

Heat Effects. Prevented by ample, cool drinking water containing 0.6 gm. sodium chloride total and additional sodium chloride in food. Morton, Tr. Roy. Soc. Trop. Med. & Hyg., 37: 347 (May) 1944.

Post-operative Intolerance Relatively small excesses not tolerated by many. Should give no isotonic saline solution day of anesthesia or on two consecutive days. In marked extracellular fluid loss, 0.5% sodium chloride + 50 gm/liter dextrose, after control of urinary suppression should determine type of solution required. Collier et al., Ann. Surg., 119: 533 (Apr.) 1944.

Muscle Spasm. Symptoms cleared completely 30 minutes after 10 gm in 200 ml. of warm water given, followed by 7 gm in one-third of patients. Gregson, Brit. M. J., II. 819 (Dec. 23) 1944.

CHLORINATED MONONITROPARAFFINS

Rabbits--

1,1-dichloro-1-nitroethane Lethal dose was 0.15 to 0.20 gm/kg. It was a skin irritant, and a lung irritant, causing edema in high concentrations. Exposure to more than 0.3 mgm. per liter for more than one hour was dangerous. Machle et al., J. Indust. Hyg. & Toxicol., 27: 95 (Apr.) 1945.

1-chloro-1-nitropropane Lethal dose was 0.05 to 0.1 gm/kg. Not a skin irritant, but a lung irritant. Ibid.

CHLOROBIPHENYL

(Sovol)

Rats—

Toxicity: Repeated exposure to concentrations of 0.2–0.3 mgm. per liter caused liver atrophy and leucocytosis followed by leucopenia. Rozenova, *Farmakol i Toksikol.*, 6: 48; 1943.

CHLOROBUTANOL**Calves—**

Dermatosis: One gm. daily after subcutaneous injection of three mgm. ascorbic acid improved dermatosis of ears, cheeks, neck and shoulders associated with low ascorbic acid blood levels. Cole, Rasmussen, and Thorp, *Vet. Med.*, 39: 204 (May) 1944.

CHLORO-HEXYL-META-CRESOL

Insecticide: Hydro-alcoholic solutions and aqueous soap emulsions at 1 and 2.5%. *Toxicity:* rats 6 ml/kg., orally, fatal; mice, 4 ml/kg. subcutaneously. Chin and Anderson, *Peking Nat. Hist. Bull.*, 16: 245; 1941; through *Exper. Stat. Record*, 86: 245 (Feb.) 1942.

**2-CHLORO-7-METHOXY-5-(8-DIETHYLAMINO-BUTYL)
AMINO ACRIDINE****Monkeys (2 kg.)—**

Malaria: 5–25 mgm. daily for three days had powerful parasitocidal action on *P. knowlesi*. Siddons and Bos, *Indian M. Gaz.*, 79: 101 (Mar.) 1944; through *Trop. Dis. Bull.*, 4: 826 (Oct.) 1944.

**1-(p-CHLOROPHENYL)-5-ISOPROPYL-5-METHYLBIGUANIDE
ACETATE
(4430)****Man—**

Plasmodium vivax infection: Orally, dosage ranging from 20 mgm. three times a day for seven days to 1 gm. three times in one day was rapidly effective in controlling clinical attacks but did not eradicate the infection. Side reactions were absent with dosage under 1 gm. daily, but nausea and vomiting occurred at higher doses. Adams, Townshend, and King, *Ann. Trop. Med.*, 39: 217 (Dec.) 1945.

2-p-CHLOROPHENYLGUANIDINE-4-B-DIETHYLAMINO-ETHYLAMINO-6-METHYL-PYRIMIDINE

(3349)

Turbidimetric Determination: The drug was precipitated by potassium mercuriiodide, opacity remained stable for four to ten minutes. Accuracy was within 10% and a minimum of two micrograms could be determined in biologic material Spinks, Ann. Trop. Med., 39: 182 (Dec.) 1945.

Man--

Therapeutic Action: Oral doses of 0.2 gm. of the dihydrochloride were given three times a day for seven days to six patients with *Plasmodium vivax* infection. Temperatures fell permanently within 24 to 72 hours. Parasites disappeared in 48 to 96 hours. The same dose was effective to 17 patients with acute benign tertian malaria. Repeated administration of 0.2 gm. three times a day for two successive days each week for six weeks had no ill effects. Adams and Sanderson, Ann. Trop. Med., 39: 165 (Dec.) 1945.

Tertian Malaria: Orally 0.2 gm. dihydrochloride three times a day for seven days effectively controlled benign and malignant tertian malaria. Relapse occurred in 70% of the former and 50% of the latter cases. The drug had no gametocidal activity against *Plasmodium vivax* or *P. falciparum*. Frontal headache, mild colic and diarrhea occurred but no renal involvement, drug-sensitivity, or effect on the blood was observed. Adams and Sanderson, Ann. Trop. Med., 39: 173 (Dec.) 1945.

Comparison with Quinacrine: Oral dosage of 0.2 gm. of drug #3349 three times a day daily or higher doses for varying periods was equally active as oral 0.2 gm. quinacrine three times a day for two days and then 0.1 gm. three times a day for five days in control of acute attacks of *Plasmodium vivax* infection. Adams and Sanderson, Ann. Trop. Med., 39: 180 (Dec.) 1945.

Excretion: 4% of 500 mgm. of the dihydrochloride, given twice daily for four to five days to four adult males, was excreted in the urine. No evidence of breakdown of the pyrimidine ring or of conjugation of the drug or formation of a phenol derivative with sulfuric acid was found. Spinks and Totter, Ann. Trop. Med., 39: 197 (Dec.) 1945.

p-CHLORO-M-XYLENOL

Man--

Excretion: Drug was not found in free form if urine was acid after intravenous injection. Drug content up to 50 mgm/100 ml. and recov-

eries up to 8.3% were obtained by alkalization of the urine with sodium bicarbonate. Drug concentration above 30 mgm/100 ml. rendered the urine bactericidal. Decomposition of urine was prevented with drug concentration above 2 mgm/100 ml. 31% of drug was excreted as equal amounts of glucuronide and sulfate ester. Zondek and Shapiro, *Biochem. J.*, 37: 592; 1943.

Animals (various)—

Blood Levels: Seldom exceeded 1 mgm/100 ml. even after large doses. Maximum blood level found from one to five hours following administration; none found in cerebrospinal fluid; absorption slow and incomplete even 48 hours after administration. *Ibid.*

CHLOROFORM

Rats—

Rhythmic Liver-fat Changes: 0.5 ml. of 10% chloroform caused appearance of fat in 12 hours; with higher concentrations, in 24 to 36 hours, reappeared abundantly in 72 to 96 hours. Knocker and Mandelstam, *Nature*, 154: 148 (July 29) 1944.

Maximum Deaths: After 4 ml. 20% chloroform, either at 24 to 36 hours or at 72 to 96 hours. *Ibid.*

Man—

Toxicity: An immediate fall in blood pressure caused by cardiac failure followed chloroform anesthesia only. Anesthesia of two hours duration caused liver damage requiring six weeks for restoration to normal. Price, *Brit. M. J.*, I: 263 (Feb.) 1944.

CHLOROPHYLL

Man—

Burn Treatment: Local use of one per cent in a bismuth subnitrate ointment decreased the healing time of deep burns. Collings, *Am. J. Surg.*, 70: 58 (Oct.) 1945.

Burns and Ulcers: 1% ointment containing 10% benzocaine, and 33.2% urea caused healing with minimum or no scar tissue formation in half of usual time required. Finkel and Levine, *Indust. Med.*, 14: 730 (Sept.) 1945.

CHLOROQUINE

(7618)

Man—

Antimalarial Therapy: Superior to quinine and quinacrine in control of acute attacks of vivax malaria. 0.3 gm. given when diagnosis was estab-

lished were repeated four hours later; then on each of following three mornings to total dose of 1.5 gm. in four days. Absence of cinchonism, longer interval before relapse and complete abolition after short remission. Most et al., J.A.M.A., 131: 963; 1946.

CHOLESTEROL

Rabbits—

Blood Concentration. Weekly ingestion of 4 gm. for eight weeks followed by 4 gm. with peanut oil for 17 weeks caused a 240–950% rise. Dijodol (9, 10-di-iodoricinostearolic acid) in doses equivalent to 0.2–0.4 gm. potassium chloride, for 12 weeks to hyperlipoidemic animals increased blood-cholesterol levels from 457–2,000 mgm. per cent. Polano, Arch. internat. de pharmacodyn. et de therap., 68: 1 (Sept.) 1942.

CHOLINE

Chicks—

Growth: 0.06% betaine—irreplaceable choline and 0.14% replaceable choline required in diet for optimal gains. Almquist, Science, 103: 722; 1916.

Mice—

LD₅₀: Intraperitoneally, 320 mgm/kg in 2% solution. Hodge and Goldstein, Proc. Soc. Exper. Biol. & Med., 51: 281 (Nov.) 1942.

Rats—

LD₅₀: Orally 6.7 gm/kg Ibid.

Acute Oral Toxicity. (413 albino) Choline chloride given by stomach tube increased in toxicity with increased concentration. LD₅₀ for two higher concentrations (average, 580 mgm/ml.) was 3.4 gm/kg; for two lower concentrations (average 300 mgm/ml.) was 6.1 gm/kg. Neumann and Hodge, Proc. Soc. Exper. Biol. & Med., 58: 87 (Jan.) 1945.

Phosphatide Choline. Remained constant. Rate of choline replacement in phosphatides dropped to 1.3 mgm. per day when no choline was fed against 3.9 mgm. per day when choline was fed at level of 50 mgm. per day. Boxer and Stetten, J. Biol. Chem., 153: 617 (May) 1944.

Spectrophotometric Determination. Based on the ultraviolet absorption of choline reinckate in acetone, using light of wavelength 327 mμ. Accuracy is ±5% for samples containing 50–100 micrograms of choline chloride. Winzler and Meserve, J. Biol. Chem., 159: 395 (July) 1945.

Growth: 1% in diets or water depressed growth. No weight was gained in animals drinking 4% solution or in those fed 10% in diet. Seven of them died from drinking 6.7% or 10% solution. Hodge, Proc. Soc. Exper. Biol. & Med., 58: 212 (Mar.) 1945.

Acute Intraperitoneal Toxicity: LD₅₀'s were mgm/100 gm. body weight: 29-34 for a solution containing 200 mgm/ml.; 37-38 for a solution of 100 mgm/ml.; 41-49 for a solution of 40 mgm/ml.; and 59-75 for a solution of 20 mgm/ml. Hodge, Proc. Soc. Exper. Biol. & Med., 57: 26 (Oct.) 1944.

Rabbits—

Dose Level Effects: 10-100 mgm/kg. in gradually increased amounts caused no change in behavior or blood condition, but 500 mgm/kg. daily for five days was lethal to one of three. Livingstone and Witts, Brit. M. J., II: 664 (Nov.) 1945.

Dogs—

Fatty Livers: 36 mgm/kg. daily was preventive dose in depancreatized animals maintained with insulin. Entenman and Chaikoff, J. Biol. Chem., 138: 477 (Apr.) 1941.

Deficiency: 50-100 mgm/100 gm. ration prevented deficiency such as: fatty degeneration and infiltration of the liver and atrophic changes of the thymus. Dutra and McKibbin, J. Lab. & Clin. Med., 30: 301 (Apr.) 1945. Treatment with 6.65 gm. or 2.38 gm. orally, over five to ten days in addition to 200 mgm.% in ration showed striking improvement in liver function and body weight. McKibbin et al., J. Lab. & Clin. Med., 30: 422 (May) 1945. Addition of 0.7% d,l-methionine or 0.1% choline chloride prevents deficiency symptoms. McKibbin, Thayer, and Stare, J. Lab. & Clin. Med., 29: 1109 (Nov.) 1944.

Hyperchromic Anemia: Orally, 10 mgm/kg. three times a day to five dogs produced 30-43% reduction in red blood cell count.

Excessive Ingestion: 40 gm. daily for six days did not increase either the free or total choline content of liver, kidney or plasma. Luecke and Pearson, J. Biol. Chem., 158: 561 (May) 1945.

Requirement of Young Pup: 50 mgm/kg. daily. McKibbin, Thayer and Stare, J. Lab. & Clin. Med., 29: 1109 (Nov.) 1944.

Hemolytic Anemia: 10 mgm/kg. choline chloride + 60 gm. fat twice daily caused rapid reduction of 20-37% in red cells count. Davis and Gross, Am. J. Physiol., 144: 444 (Aug.) 1945.

Man--

Retinal Lesions: 0.3 gm. three times daily for two weeks controlled ocular hemorrhage. Dimitry and Lombardo, *Am. J. Ophth.*, 28: 902 (Aug.) 1945.

Reticulocytosis. 400 mgm choline + 125 gm. butter to breakfasts of two caused decrease in red cells for 36 hours followed by reticulocytosis. Davis and Gross, *Am. J. Physiol.*, 144: 444 (Aug.) 1945

Therapy of Liver Cirrhosis. Orally 4 gm in divided doses daily for five months were administered to two patients and 1 gm choline and 1 gm. inositol six times daily for four months in another. Goldstein and Rosahn, *Conn. M. J.*, 9: 351 (May) 1945.

Hepatorenal Syndrome. Oral and continuous intravenous drip of 28 gm. given; three doses of 10 gm. each of methuonine was substituted after the third day because of rash. Recovery followed. Barclay and Cooke, *Lancet*, 249: 458; 1945.

Liver Cirrhosis 17 mgm/kg. daily for 70 days failed to augment macrocytic anemia and progressively increased red cells and hemoglobin values in a man with cirrhosis of the liver. Watson and Castle, *J.A.M.A.*, 129: 802; 1945.

Infective Hepatitis: Improved with 2 gm per day for two weeks in a patient. In atrophic cirrhosis 5 gm three times a day for five weeks was not beneficial to one woman and caused persistent nausea in another. Livingstone and Witty, *Brit. M. J.*, II 66 (Nov) 1945.

CHOLINE ACETYLASE

Biosynthesis of Acetylcholine. One gm. fresh rat brain yielded an enzyme solution in presence of adenosine triphosphate under strictly anaerobic conditions from which 100-150 micrograms acetylcholine were formed per hour. Nachmanson, *Proc. Soc. Exper. Biol. & Med.*, 57: 361 (Dec.) 1944.

CINCHOPHEN

Dogs--

Effect of Bile-acids 50% of 24 hour dosage recovered in bile when conjugated, unoxidized cinchophen bile acid were given, 50% average daily recovery with use of unconjugated, oxidized cholic acid, 43% recovery in controls. Annegers et al, *Gastroenterology*, 2: 138 (Feb) 1944.

Man--

Non-toxicity to Arthritic Patients (100) Hippuric acid total and free cholesterol determinations, icterus index showed 1/100 impaired liver

lunction. Eaton, Olivetti and Hayden, J. Am. Inst. Homeop., 34: 565 (Dec.) 1941.

CITRININ

Mice—

Toxicity: Intraperitoneally, 2 mgm./0.5 ml. lethal to 20 gm. mice. All survived 1 mgm. per injection. Timonin, Canad. Pub. Health J., 35: 92 (Feb.) 1944.

CITRONELLA

(Oil extracted from leaves of a Congo plant, family Cymbopagon, containing 65% of a mixture of geraniol, citronellol, citral and citronellal.)

Man—

Leprosy: One part diluted with nine parts of cottonseed oil and given subcutaneously or intramuscularly, 1 ml. (daily) the first week, 2 ml. the second week, then 3 ml. for ten weeks, followed by a rest of 15 days, was used on 2,328 patients. 114 were arrested, 223 improved, 95 became worse and the rest remained stationary. Degotte, Leprosy Rev., 15: 28 (Dec.) 1944; through Trop. Dis. Bull., 42: 394 (May) 1945.

CLAVICIN

Tropical Fish and Paramecia—

Toxicity: 1:1,000,000 and 1:100,000 dilution killed. Katzman et al., J. Biol. Chem., 154: 475 (July) 1944.

Mice—

Toxicity: LD₅₀ subcutaneously, 0.2 mgm. per 20–25 gm. mouse. Ibid.

Tetanus Toxin: Rendered non-toxic with 2 mgm. and a slight reduction of toxicity by 0.2 mgm. Neter, J. Infect. Dis., 76: 20 (Jan.-Feb.) 1945.

Rats—

Toxicity: LD₅₀ subcutaneously, 5.0 mgm. per 200 gm. rat. Katzman et al., J. Biol. Chem., 154: 475 (July) 1944.

Toxic Reactions in Mice and Rats: Severe edema of lungs, fluid in abdomen and thoracic cavities, hyperemia, marked urinary retention with no extensive kidney damage and necrosis at site of injection. Ibid.

Dogs—

Effect: Intravenously, 25 mgm into 7 kg. dog caused temporary stoppage of heart beat, followed by resumption at low rate and then by an increase of heart beat and carotid pressure above normal; response was temporarily depressed and then rose above normal. Ibid.

CLORARSEN

(3-amino-4-hydroxyphenyldichlorarsine-hydrochloride+sodium citrate)
Man—

Syphilis: Beneficial to 47 of 50 who had had intestinal upset after mapharsen injections. *Dosage*. 0.067 gm. *Reactions*: Less severe than after mapharsen. Minor reactions followed intravenous use of 1.34 gm, e.g., nausea, vomiting, fever, headache or toxic erythema Kalz et al., *Canad. M. A. J.*, 50: 237 (Mar.) 1944.

CLOSTRIDIUM NOVI TOXOID

Sheep—

Infectious Necrotic Hepatitis Subcutaneously, 5 ml. alum precipitated toxoid protected five sheep against *Clostridium novyi* toxin 34 months later, two given 15 mgm per kg. and three given 15, 8.3, and 8.2 mgm/kg respectively. Immunity to 80 mgm toxin per kg. existed 45 months after vaccination in eight sheep and 56 months in one. Tunnicliff, *J. Am. Vet. M. A.*, 103: 368 (Dec) 1913.

COCAINE

Qualitative Determination—

Schorl's Method for determining benzoic acid in cocaine: Evaporate a sample with fuming nitric acid, reduce with aluminum and stannous chloride, and treat with sodium nitrate. On addition of 1,8-dihydroxynaphthalene-3,6-disulfonic acid an intense red violet color was produced. The reaction was specific and 2 mgm gave a definite test Malowan, *J. Am. Pharm. A. (Scient. Ed.)*, 34: 245 (Sept.) 1945 (Sec estradiol benzoate.)

Frog Heart—

Effect: Stimulated in dilution of $>100,000$. Suzuki, *Fukuoka Acta med.*, 34: 42; 1941; through *Far Eastern Sci. Bull.*, 3: 55 (Dec.) 1943. Intravenously, 0.1-1.0 mgm/kg. increased apex beat and amplitude. 5 mgm/kg. or more interfered with cardiac cycle producing partial dilatation, and slowing of beat and arrhythmia. 20,000 times dilution constricted the arteries, and 2,000-10,000 dilution dilated the arteries. *Ibid.*

Mice (white)—

Toxicity: MLD was 85 mgm/kg. when cocaine given intraperitoneally. Co Tui et al., *Anesthesia and Analgesia*, 22: 301 (Nov. and Dec.) 1913.

Guinea Pigs—

Antagonist. Epinephrine, 1 100,000-1 25,000 prevented convulsions

with simultaneous subcutaneous injection of 1 ml. 4% cocaine per kg.: 1:5,000 concentration of epinephrine enhanced cocaine toxicity. Craver, Proc. Soc. Exper. Biol. & Med., 58: 128 (Feb.) 1945.

Rabbits—

Blood Pressure: Intravenously, 0.1–1.0 mgm/kg., blood pressure was increased and then decreased, and decreased from beginning with 5 mgm/kg. or more. Subcutaneously, 0.5–3.0 mgm/kg. increased blood pressure first and then decreased. See Suzuki, 1941.

Corneal Anesthesia: Anesthetic duration of 0.05 M (1.7%) solution was shortened 10% by a 1% aqueous alcohol yeast extract solution and 20% by a 5% extract. Cook, Proc. Soc. Exper. Biol. & Med., 54: 203 (Nov.) 1943.

Man—

Poisoning: Acute, non-fatal poisoning with 0.4 gm. single dose (3 cases). 0.4 gm. three times in 3.5 hours (1 case). Alwall, Acta med. Scandinav., 106: 335 (Feb. 17) 1941.

CODEINE

Man—

Intractable Pain: 60 mgm. every 90–120 minutes controlled. Seevers, Wisconsin M. J., 41: 113; 1942.

COD LIVER OIL

Man—

Bladder Instillations: After lavage with 1:1,000 potassium permanganate, 60 ml. doses given at three to seven day intervals (assayed 1,800 and 180 U.S.P. units vitamins A and D respectively). Ewart and Hoffman, Lahey Clinic Bull., 4: 27 (July) 1944.

Therapy of cutaneous and genito-urinary tuberculosis by topical application. Banyai, Urol. & Cutan. Rev., 46: 72 (Feb.) 1942.

Burn Therapy: Sterile cod liver oil bandages without previous disinfection to burns of all degrees Tetanus antitoxin and vitamin C given. Compared to tannin therapy (see tannic acid) cod liver oil proved satisfactory in every respect. Deuts. Milit., 6:287 (May) 1942; through J.A.M.A., 119: 982; 1942.

Frostbite Therapy: Initial therapy with continuous wet dressings and cod liver oil ointments applied during night. When areas were clean, topical use of bismuth subgallate used. Plech, M. Klin., 39: 351 (Apr.) 1943; through Bull. War Med., 4: 201 (Dec.) 1943.

Tropical Ulcer. 15 gm. cod liver oil three times daily (25, 200 Inter-

national Units Vitamin A) caused recovery in 74% of 27 patients. Charters, Tr. Roy. Soc. Trop. Med. & Hyg., 37: 205 (Dec.) 1915.

COLCHICINE

Man—

Poisoning: Fatal in seven to 11 days to two patients given 13 and 29 mgm. respectively over four and seven days. Agranulocytosis, aplastic anemia and probably peripheral neuritis were due to the drug. Another patient, given 28 mgm. over 61 days with several rest intervals, showed early marked decrease in tumor size, thereafter unaffected, and death occurred after 19 days when drug was discontinued. Brown and Seed, Am. J. Clin. Path., 15: 189 (May) 1915.

Myelogenous Leukemia: Orally, 0.5 mgm. three times daily, then twice daily for 13 months produced temporary benefit. Diarrhea when dosage was > 1 mgm. Kneedler, J A M A., 129: 272; 1915.

COPPER

Dogs—

Hemoglobin Production in Experimental Anemia: Five mgm. per day produced response. 10-15 mgm. per day caused 22 gm. hemoglobin output after two weeks feeding. Robscheit, Robbins, and Whipple, J. Exper. Med., 75: 481 (May) 1912.

Man—

Metabolism and Requirement: With average intake of 2.65 mgm. on self-chosen diet by 65 women, average daily retention was 0.85 mgm.; four on constant diet, with average intake of 2.14 mgm., retention was 0.23 mgm. Requirement—2.0-2.5 mgm. copper daily. Leverton and Binkley, J. Nutrition, 27: 45 (Jan) 1911.

COPPER UNDECYLENATE

Man—

Saturated solution in carbowax cleared 57% of children infected with *Tinea capitis* who received 38 to 40 treatments. Schwarz et al., Pub. Health Bull., #291, 1916.

CORTICAL EXTRACT

Dogs—

Shock Therapy: Intravenously or intramuscularly, 0.5-2.0 cc/1g. Helfrich, Cassels, and Cole, Am. J. Surg., 33: 410 (Feb.) 1912.

Man—

Shock Therapy: Intravenously or intramuscularly, divided doses of 6–10 ml. 1.5 and 0.5 hour before major operation. Minimized changes preliminary to shock development. Ibid.

CORTIN**Man—**

Hyperinsulinism: 30 ml. daily was incapable of raising blood sugar level or exerting anti-insulin effect. Conn and Conn, Arch. Int. Med., 68: 1115 (Dec.) 1941.

Addison's Disease: Intravenously, 1,500–2,500 dog units per day for three days caused no acceleration of sodium storage. In normals, storage occurred. Greene, David, and Johnston, J. Clin. Endocrinol., 2: 49 (Jan.) 1942.

COSMETICS**Man—**

Safety Test: Two patch tests approximately two weeks apart should be done on at least 200 individuals. Same 200 should use product for four weeks. Schwartz and Peck, Pub. Health Rep., 59: 546; 1944.

CRESYLIC ACIDS**Mice—**

LD₅₀: Locally on skin, 1.0 ml/kg. of common coal tar cresylic acid, soluble cresylic disinfectant, common soluble cresylic disinfectant, U.S.P. saponified cresol solution. Campbell, Soap & Sanitary Chems., 17: 103 (Apr.) 1941.

CUMENE

(Isopropyl benzene)

Mice—

Toxicity: MLD: 10 mgm/L. (2,000 p.p m.) Produced narcosis more slowly but longer lasting than benzene or toluene. Mice exposed to cumene showed moderate fat deposition in liver and kidney and phagocytosis of nuclear fragments in spleen. Majority died within 8 to 24 hours. Werner, Dunn, and von Oettingen, J. Indust. Hyg. & Toxicol., 26: 264 (Oct.) 1944.

CURARE**Dogs—**

Effect on Smooth Muscle: Given in 0.001 gm/kg., the peristalsis of the small intestine ceased and did not regain muscular tone for considerable time. Gross and Cullen, Anesthesiology, 6: 231 (May) 1945.

Prolonged Curarization by intravenous injection of 9-30 ml. (Intocostin) standardized purified extract of curare caused death within 45 hours despite maintenance of respiration. All animals showed dilatation of heart at autopsy. Administration of atropine intravenously with curare prevented dilatation of heart but death occurred and administration of pilocarpine (1 mgm/0.5 hour subcutaneously) or ergotamine did not prevent death. Perlstein and Weinglass, *Am. J. Dis. Child.*, 67: 360 (May) 1944.

Respiration: Intravenously, 2-5 ml. in anesthetized dog produced, after a short interval of respiratory excitation, a decrease of respiratory frequency and amplitude; this inhibition was progressive. Fegler, *J. Physiol.*, 100: 417 (Mar.) 1942.

Man—

Fasciculations. Intravenously given 2 ml. curare extract abolished spontaneous muscular fasciculations in four patients. Since curare blocks impulses at the myoneural junction, abolition of fasciculations indicates that they originate at this point or proximal to it and not in the anterior horn cells. Neostigmine, 2.5-3 mgm. given intramuscularly did not counteract curare. Forster and Alpers, *Arch. Neurol. Psychiat.*, 51: 264 (Mar.) 1944.

Poliomyelitis. 0.9 mgm/kg of Intocostin obtained striking improvement in four patients with acute anterior poliomyelitis. Ransohoff, *J.A.M.A.*, 129: 129; 1945. 1 mgm/kg. could usually be tolerated. More may be needed for adequate relaxation. Not used initially with neostigmine, but one may be used to counteract an excess of the other. Orth, *Wisconsin M. J.*, 41: 993 (Oct.) 1945.

Cauda Equina Lesions: 10-100 mgm used to control pain. Braden, *J.A.M.A.*, 129: 151; 1945.

Relaxation: Intravenously, 3 ml. curare extract (Intocostin) to average adult produced good relaxation prior to light second plane cyclopropane anesthesia. If insufficient, 1.5-2 ml. was given in 3 to 5 minutes. Another injection of 1.5-2 ml. facilitated closure of peritoneum in operations lasting more than 45 minutes. Cullen, *Anesthesiology*, 5: 166 (Mar.) 1944. Intravenously 60-80 units (optimum dose 70 units) at moment of abdominal incision and additional 20-40 units if operation required more than 30 minutes in sodium pentothal, nitrous oxide and oxygen anesthesia. Brady, *Anesthesiology*, 6: 581 (July) 1945. Intravenously 60-100 mgm for adult with cyclopropane, 20-40 mgm curare (1-2 ml. Intocostin) with ether. Griffith, *Lancet*, 249: 71 (July) 1945. Intravenously 3 ml. Intocostin (60 mgm. curare) in 1-2 min-

utes to a maximum dose of 10 ml. for complete abdominal relaxation in presence of light (second plane) anesthesia. Mallinson, *Lancet*, 249: 75 (July) 1945. 20-40 mgm. repeated at five minute intervals until relaxed in cyclopropane or ether-cyclopropane anesthesia. Average total 100 mgm. Whiteacre, Fisher, *Ohio State M. J.*, 40: 1155 (Dec.) 1944.

100 mgm. after anesthesia with nitrous oxide was satisfactory. Extreme respiratory depression was rare or brief. Waters, *Anesthesiology*, 5: 618 (Nov.) 1944. Intravenously, 100 mgm. (5 ml. Intocostrin) in 90 patients overcame inadequate relaxation in surgery. Effect within a few seconds, reached climax in five minutes and lasted 15-20 minutes. Griffith, *Canad. M. A. J.*, 50: 144 (Feb.) 1944.

Anesthesia: Intravenously, 300 units, slowly in divided doses in conjunction with available gaseous anesthetics produced no untoward effects. Lundy et al., *Proc. Staff Meet. Mayo Clin.*, 20: 292 (Aug.) 1945.

Adjuvant to Anesthesia: Average initial dose of 0.0686 gm. intravenously and average total dose of 0.0775 gm. pre-operatively were administered to supplement cyclopropane anesthesia. Maximum effect was obtained in 1-2.5 minutes; muscular relaxation lasted 20-120 minutes. Smith, *Rocky Mountain M. J.*, 41: 313 (May) 1944.

Clinical Uses: Intravenously, 100 mgm. caused complete muscular relaxation and was advantageous in peritoneal closure. Best results obtained with cyclopropane; curare dose was reduced to $\frac{1}{3}$ with ether because of synergism. 1 mgm/kg. given intravenously prior to administration of convulsant, produced maximum degree of relaxation. Danger: Possibility of respiratory embarrassment. If it occurred, artificial respiration was given immediately; 1 ml. prostigmine in 1:2,000 solution was antidotal. Beddingfield, *Mod. Hosp.*, 65: 88 (July) 1945.

General Anesthesia: Intravenously, 4-5 ml. curare extract (1 ml. containing 20 mgm. active curare substance) increased skeletal muscle relaxation in light cyclopropane anesthesia. (Dosage was 10-20 mgm. per 9 kg. body weight by rapid injection.) Griffith and Johnson, *Anesthesiology*, 3: 418 (July) 1942.

Supplement in Anesthesia: 0.3-5 ml. (average 3 ml. intravenously, gave better muscular relaxation in general anesthesia with cyclopropane, with pentothal alone or with cyclopropane or nitrous oxide and with ether. Hudon, *Laval méd.*, 9: 242 (Apr.) 1944.

Endoscopy: Recommended dosage: 0.5 mgm/0.5 kg. body weight less 20 mgm., increased at two minute intervals by 10 mgm. Morphine pre-

medication omitted. Silverberg et al., New York State J. Med., 44: 2468 (Nov. 15) 1944.

Respiratory Paralysis Occurred with 45 mgm. (child). Silverberg et al., New York State J. Med., 41. 2468 (Nov. 15) 1944.

Respiratory Recovery Proper respiration followed or was established only four hours after an operation lasting 25 hours and requiring 150 mgm. Whiteacre, Fisher, Ohio State M. J., 40: 1155 (Dec.) 1944.

Modification of Therapeutic Convulsions Initial dose was 10 mgm. per 9 kg. body weight intravenously, minus 1 ml. (20 mgm. active principle in 1 ml.). If tolerated, but insufficient, then 10 mgm/9 kg. or 15 mgm/9 kg. was given at an injection rate of 30-60 seconds. Electric shock was given while curarization was at its peak. Jones and Pleasants, Diseases of the Nervous Syst., 4: 17 (Jan.) 1913.

Foetus Unaffected. 150 mgm intravenously to mother for labor. Whiteacre, Fisher, Ohio State M. J., 40: 1155 (Dec.) 1944.

Spastic Children 0.9-3.3 mgm/kg. given intramuscularly was optimal maintenance dose at four day intervals. Denhoff and Bradley, New England J. Med., 226 411, 1942.

CURARINE CHLORIDE

Man—

Relaxation. Curarine chloride was more potent than intocostrin; dose should not exceed 70 mgm. Approximately 30 mgm. was adequate for lower abdominal operations. MacIntosh, Lancet, 219: 121; 1915.

CYANAMIDE

Rats—

Parasympatheticomimetic Response Intraperitoneally, 200 to 400 mgm/kg. caused initial miosis, followed in 15 minutes by moderate mydriasis. Fibrillary twitching, lachrimation and coma occurred with death in three to six hours. Barnard, Proc. Soc. Exper. Biol. & Med., 54: 251 (Nov.) 1913.

With Atropine 0.3 mgm atropine kg immediately after cyanamide prevented initial miosis, increase in intra-orbital pressure, lachrimation, fibrillary twitching and bronchorrhea, but not coma. Ibid.

CYANIDE

Rats (young)—

Tolerated 5 mgm sodium cyanide given subcutaneously for 50 minutes. Himwich, Fazekas, and Alexander, Proc Soc Exper Biol. & Med., 46: 553 (Apr.) 1941.

Rats (adult)—

Acute Toxicity: 5 mgm. sodium cyanide given subcutaneously caused death in ten minutes. Ibid.

CYCLOHEXANE

(Methylcyclohexane and derivatives)

Rabbits—

Toxicity: 39.55 and 42.5 mgm/liter air of methylcyclohexane and cyclohexane respectively caused convulsions which occurred at 4 mgm. cyclohexane/liter air. Fatalities occurred after repeated exposure to following concentration in mgm/liter: 4.0 cyclohexanol, 12.12 cyclohexanone, 25.1 cyclohexane, 28.75 methylcyclohexane. Maximum safe concentration in mgm/liter for lengthy exposure, 4.57–11.35 methylcyclohexane; 1.46–2.65 cyclohexane; 0.82–2.31 methylcyclohexane; below 0.75 cyclohexanone; below 0.58 cyclohexanol; below 0.56 methylcyclohexanol. Treon et al., J. Indust Hyg. & Toxicol., 25: 323 (Oct.) 1943.

CYCLOPLEGINA

(Benzyl oil-diethylamino ethanol)

Animals—

Cycloplegic Action: Occurred with 3% solution within 20 minutes and lasted an average of eight hours. Americano and Rocha, Ophthalmos, 3:287; 1944; through Am. J. Ophth., 28: 924 (Aug.) 1945.

CYCLOPROPANE**Dogs—**

Blood Pressure: 50% and 75% with oxygen given intratracheally for five minutes to animals previously medicated with 0.1 gm/2.25 kg. pentobarbital caused slight initial rise in blood pressure; fell for two minutes and then rose during third and fourth minutes. After discontinuing anesthesia, a steep rise occurred for 20 seconds, followed by a fall for ten seconds. Brace, Scherf, and Spire, Anesthesiology, 2: 261 (May) 1941.

Dogs and Cats—

Post-hemorrhage Anesthesia: 25 to 30% blood volume was withdrawn from 16 dogs and three cats in five to seven minutes. After cyclopropane anesthesia (30 to 50% mixture with oxygen): arterial blood pressure was 120 mm. Hg before and 64 mm. after hemorrhage; 104 mm. during anesthesia. Pulse pressure: 58 mm., 8 mm., 44 mm., respectively. *Pulse Rate:* Increased from 87 to 174 in dogs, and from 210 to 303 in cats after hemorrhage, fell to an average 71 in dogs and 157 in cats during anesthe-

sia. All animals survived surgical anesthesia. Hershey and Rovenstine, *Proc. Soc. Exper. Biol. & Med.*, 54: 68 (Oct.) 1943.

Man—

Anesthesia: 0.01 gm. morphine and 0.0045 gm. atropine given one-half hour before pelvic surgery with cyclopropane, atropine one-half hour before operation and morphine when patient started for operating room. High amount of oxygen with cyclopropane was an advantage in cesarean section. Brockman, *Bull. Am. A. Nurse Anesthetists*, 12: 13 (Feb.) 1944.

CYCLOPROPYL VINYL ETHER

Mice, Rats, Dogs, and Monkeys—

Potency approximated that of chloroform, anesthetic index more than twice that of ethyl ether. Only monkey's heart slightly depressed in rate and amplitude. Explosive range same as for ether. Oil/water coefficient 16 times greater than ethyl ether, anesthetic concentrations in blood 1/5 those of ether. Krantz et al., *J. Pharmacol. & Exper. Therap.*, 75: 30 (May) 1942.

Man—

20 anesthetics given without untoward reactions. *Ibid.*

CYSTINE

Cats—

Achromotrichia: On a diet containing 18% casein, black cats became grey in four to five weeks. Diminution of greying with 200 microgram pantothenic acid starting from four to five weeks to a maximum after 12 to 14 weeks. Addition of 75 mgm. cystine daily to pantothenic acid supplement. Final stage of regeneration in five to seven weeks. Pavcek and Baum, *Proc. Soc. Exper. Biol. & Med.*, 47: 271 (June) 1941.

Man—

Dermatitis: 0.25 gm. cystine hydrochloride subcutaneously and 1 gm. cystine orally to respective totals of 2 and 10 gm. in one patient and 1 gm. cystine orally for 20 days in second patient improved severe exfoliative dermatitis. Peters, *Lancet*, 248: 264; 1945.

CYVERINE

(di-(β -cyclohexyl ethyl) methylamine)

Man—

Alopecia, exfoliative dermatitis and perspiration diminished after 800 mgm. of the hydrochloride in 16 days, followed after nine day interval by 120 mgm. in three days. Numbness in arms developed after 800 mgm. Levin and Behrman, *J.A.M.A.*, 118: 41 (Jan. 3) 1942.

D. B. E.

(α -di(p-ethoxyphenyl) β -phenyl bromo ethylene 1-bromo-2,2-diphenethyl-1, 1-phenyl ethylene)

Mice—

Fate: 2 mgm. dissolved in 0.2 ml. sesame oil given to ovariectomized mice. More than one-half of drug disappeared within 24 hours, but more than 20% recovered on third day and five to ten per cent one week later. Liver contained not > 0.4 mgm.; muscle, 2 mgm.; fat, 15 mgm.; and uterus, 2 mgm. estrogen/100 gm. Excretion up to 10% within first few days. Robson and Ansari, J. Pharmacol. & Exper. Therap., 79: 340 (Dec.) 1943.

D. D. T.

2,2-bis(p-chlorophenyl)-1,1,1-trichloroethane)

Insecticidal Activity: D.D.T. was one-half as effective as the methoxy analog, 1,1-di-p-anicyl-2,2,2-trichloroethane, in knocking down houseflies during ten minutes' exposure. D.D.T. and the methoxy and ethoxy analogs in concentrations of 0.03–0.04 parts per million and the n-propoxy analog at 0.4 parts per million killed half of mosquito larvae in 20 hours. Prill, Hartzell, and Arthur, Science, 101: 464; 1945.

Mosquitoes: 2% gave 100% kill against adult anopheles. Combination to increase knockdown power: 20% D.D.T. and 80% Thanite, and 40% D.D.T. and 60% Thanite gave kills of 96% and 99% respectively, and caused paralysis of 92 and 86% respectively. D.D.T. alone killed 100% and paralyzed 57%, while a pyrethrum preparation gave 97% and 94% response. Rice, Huffaker, and Back, Soap Sanitary Chem. Soc., 21: 119 (Mar.) 1945.

Mice—

Fatal: Ingestion by licking the fur in concentrations of 6.22 mgm. per liter air, except when 6% sesame oil was present: caused death preceded by increased excitation, nervousness, tremors, clonic convulsions. Daily insufflation of 100 mgm/kg. pure D.D.T. for 18 days, and repeated cutaneous application of 0.012 ml. aerosol residue were fatal. Neal, Soap. Sanit. Chem. S., 21: 99 (Jan.) 1945.

Toxic Signs: Observed when exposed to aerosols of 1–5% D.D.T. in 6% sesame oil or in 10% cyclohexanone and 85–89% Freon (dichlorodifluoromethane) once daily for more than one week. Ibid.

Subacute Toxicity: 0.05% (500 p.p.m.) in diet from three days to 20 weeks. Woodard et al., J. Pharmacol. & Exper. Therap., 82: 152 (Oct.) 1944.

Chicks (growing)—

Subacute Toxicity: Was observed with 0.05% in the diet. Woodard et al., J. Pharmacol. & Exper. Therap., 82: 159 (Oct.) 1944.

Rats—

Acute Toxicity: LD₅₀, 150 mgm/kg. LD₆₀, 200 mgm/kg. Smith and Stohlman, Pub. Health Rep., 59: 984 (July 28) 1944.

Detoxification: Animals survived 0.1% D.D.T. fed together with 0.2% cyclohexane daily for 90 days, whereas same amount alone caused high mortality from 18th day on. Ibid.

Protein Diet: Low protein diet did not alter susceptibility to liver damage but slightly increased toxicity to D.D.T. **Antidotes:** Urethane reduced mortality rate from 80% to 12.5% on intraperitoneal 1.2-2.5 gm/kg. in one to three days. Dilantin intraperitoneal 200-250 mgm/kg. was not effective, reduced mortality to 46.7%. Smith and Stohlman, Pub. Health Rep., 60: 289 (Mar.) 1945.

Rats, Rabbits, and Guinea Pigs—

Percutaneous Absorption: 0.5 ml of 30% solution of D.D.T./kg/day (150 mgm/kg/day of D.D.T.) by inunction causes death in some cases after 30 days. Reactions were anorexia, severe weight loss, hyperexcitability, nervous tremors leading to clonic convulsions. Draize, Nelson, and Calvery, J. Pharmacol. & Exper. Therap., 82: 159 (Oct.) 1944.

Guinea Pigs—

Subacute Toxicity: 0.1% in diet. Woodard et al., J. Pharmacol. & Exper. Therap., 82: 152 (Oct.) 1944.

Rabbits—

Acute Toxicity: LD₃₃, 159 mgm/kg. and LD₅₀, 330 mgm/kg. Smith and Stohlman, Pub. Health Rep., 59: 984 (July 28) 1944.

Excretion: 25 mgm. D.D.T./kg. in olive oil were given. Daily excretion increased gradually to a peak of 4-5.9 mgm. at time of death. Single oral dose of 300 or 400 mgm/kg. was excreted for 10 days; 5-50% eliminated in feces and 10-65% in urine. Smith and Stohlman, Pub. Health Rep., 60: 289 (Mar.) 1945.

Metabolite in Urine: Di(p-chlorophenyl)-2,2,2 trichloroethane. Smith and Stohlman, Pub. Health Rep., 59: 984 (July 28) 1944.

Inunction: 5% in acetone applied to ears, head, and feet caused severe and fatal toxic reactions. 0.5% solution caused transient paralysis and

muscular tremors in eight week old animals. Taylor, Lancet, 249: 320 (Sept.) 1945.

Cats—

Acute Toxicity: LD₅₀, 200 mgm/kg.; LD₆₀, 300 mgm/kg. Smith, Stohlman, Pub. Health Rep., 59: 984 (July) 1944.

Excretion: With 5 or 10 mgm/kg/day, orally, urinary excretion was lower than in rabbits. Drug detected in urine within five days, long before toxic signs appeared. Smith and Stohlman, Pub. Health Rep., 60: 289 (Mar.) 1945.

Dogs—

Fatal: Same as for mice, but survived much longer. Neal. (See Mice.)

Tolerated: Daily three hour exposures to 10% D.D.T. as a dust, a heavy mist of 1% D.D.T. Deobase mixture or to massive doses of cyclohexanone mixture. Neal (see Mice).

Goats—

Toxic Metabolite: Milk from an animal given 75 gm. (0.3 gm/kg.) killed rats fed on it in 29 to 31 hours. One week later, the toxic element was still being excreted. Telford, Soap Sanitary Chems., 21: 161 (Dec.) 1945.

Man—

Pediculosis Capitis: One application of emulsion was effective for 14–18 days, killed all lice immediately and larvae as they hatched out Scobbie, Brit. M. J., 1: 409 (Mar.) 1945.

DELVINAL SODIUM

(Sodium 5-ethyl-5(1-methyl-1-butenyl) barbiturate)

Dogs—

Surgical Anesthesia: Intravenously, 48.8 mgm/kg. effective. Induction period averaged 30 minutes; surgical anesthesia, 2.5 hours; deep sleep, 8½ hours; awakening 13 hours; ataxia, 4 hours, and total time 28 hours 12 minutes. No pre-anesthesia sedation, no annoying reaction or violent movements. Pulse and respiration rates and temperature decreased during anesthesia and returned to normal. Spleen enlarged. No development of tolerance. Allison, Seeley, and Morris, Am. J. Vet. Res., 5: 62 (June) 1944.

Monkeys (Macacus mulatta)—

Respiration: 30–45 mgm/kg. decreased the oxygen consumption. Anesthesia: 40–45 mgm/kg produced surgical anesthesia that lasted for three to five hours. Peoples and Carmichael, Proc. Soc. Exper. Biol. & Med., 48: 381 (Nov.) 1941.

Man (children)—

Sedative and Hypnotic: 0.1–0.2 gm. orally or rectally, 90 minutes before anesthesia. Freedom from after effects, no addiction or alteration in blood, urine, respiration, blood pressure, or pulse Marvin, Anes. & Anal., 21: 229; 1942.

Man—

Epilepsy: Orally, 0.1–0.2 gm. three times daily for three months brought definite improvement in mental status in 32 of 40 chronic epileptics who had not responded to other medication. Intravenously, 0.3 gm. caused almost immediate cessation of status epilepticus in three patients. Davidoff and Doolittle, Dis Nerv. System, 5: 84 (Mar.) 1944.

DESOXYCORTICOSTERONE ACETATE**Cocks (White Leghorns)—**

Local Effect: 3 mgm. total dose in oil, locally over three days on combs, increased size 81%. Morato, Manaro, Arch. Clin. Inst. Endocrinologia, 1: 343; 1937–1940.

Mice (adrenalectomized)—

Protective Action: 250 microgram and 500 microgram dose levels prolonged life in mice subjected to low temperature. Zarrow, Proc. Soc. Exper. Biol. & Med., 50 135 (May) 1942 (see progesterone).

Rats—

Repeated Administration 2 mgm. injected daily for 30 days had no effect on immature castrated animals. Morato, Manaro, Arch. Clin. Inst. Endocrinologia, 1: 343; 1937–1940.

Oral Administration: 0.09–0.33 mgm. daily maintained life and enabled adrenalectomized animals to grow on salt-free diet. Frankel-Conrat, Proc. Soc. Exper. Biol. & Med., 51 300 (Nov.) 1912

Deciduoma: 5 mgm. in 0.2 ml. peanut oil twice daily produced plus 4 deciduomata in previously castrated animal while in estrus and subjected to uterine traumatization. Masson, Proc. Soc. Exper. Biol. & Med., 54: 196 (Nov.) 1943.

Inactivation: Ten 100-day male albino rats increased sodium chloride intake following adrenalectomy 0.38 mgm daily absorption on subcutaneous insertion of pellets, caused sodium chloride intake to decrease to normal. Mark, Endocrinology, 31 582 (Dec.) 1912.

Arthritis: Produced with subcutaneous injection of 2 or 3 mgm. crystals twice daily in an aqueous suspension containing 20 mgm/ml. or 30 mgm/ml. Adrenalectomy, thyroidectomy or exposure to cold greatly

facilitated production of joint lesions. Selye et al., J.A.M.A., 124: 201; 1944.

Overdosage: 2 ml., 0.5% in two subcutaneous doses daily for two months and 1% sodium chloride as drinking water caused nephrosclerosis, cast formation in renal tubules, hypertrophy of renal arterioles, and marked cardiac hypertrophy. Selye and Hall, Am. Heart J., 27: 338 (Mar.) 1944.

Cholesterol: 6 mgm. daily produced irregular increase in unilaterally nephrectomized animals of adrenal cholesterol and 100% increase in serum cholesterol. Lemin, Endocrinology, 37: 34 (July) 1945

Diuresis: 2.0 mgm. or more - - - - - n adrenal-
- - - - - . 1.0 mgm.
- - - - - excretion from 20 to 68% and
- - - - - with epinephrine increased to 79%. Hays and Mathieson, Endocrinology, 37: 147 (Aug.) 1945.

Potassium Chloride Poisoning: 2 mgm. doses caused adrenal cortex atrophy which decreased resistance to potassium chloride poisoning. Lowenstein and Zwemer, Endocrinology, 33: 361 (Dec.) 1943.

Rats and Guinea Pigs—

Nervous System Effect: Intraperitoneally, 0.04–0.2 mgm. had exciting and 2 mgm. a depressing action on encephalomedullary centers. Muscular chronaxia decreased; <1 mgm. counteracted depressing action of vitamin C deficiency or adrenal insufficiency. Chauchard, Compt. rend. Soc. de biol., 137: 175 (Mar.) 1943.

Rabbits—

Insulin Coma: 2 mgm/kg. caused recovery. Aldama, Med., Madrid, 12: 703 (Oct.) 1944; through J.A.M.A., 127: 1022; 1945.

Dogs—

Bilaterally Adrenalectomized: Maintained good condition with low sodium chloride intake plus daily administration: 1.2 mgm. subcutaneous; 2.0 mgm. in oil; 5.0 mgm. in cocoa butter, percutaneous; 6.0 mgm. in propylene glycol, sublingual; 15.0 mgm. in propylene glycol, oral; 15.0 mgm. in cocoa butter, rectal. Thorn et al., J. Clin. Endocrinology, 1: 967 (Dec.) 1941.

Plasma Volume: Intramuscularly, 5 mgm. synthetic substance in oil for five days was more effective in increasing plasma volume in normal male dogs than sublingual administration of 15 mgm. of hormone in

propylene glycol (5 mgm. three times daily for five days). Clinton et al., *Endocrinology*, 31: 578 (Dec.) 1942.

Polydipsia and Polyuria Syndrome induced by 5-10 mgm. over four months period. Muscular weakness and lack of coordination were prominent. Mochlig and Jaffe, *J. Lab. & Clin. Med.*, 27: 1009 (May) 1942.

Man—

Addison's Disease 3-10 mgm. were given as supplement in first two to three days of Addisonian crisis. Tablets absorbed at approximately 1 mgm./day for each 300 mgm., aided in maintaining patient. If necessary, 2.5-7.5 ml. adrenal cortical extract per day was also given. If implanted tablets were absorbed, potassium level was maintained with 4 gm. potassium chloride daily or 0.12 gm. liter potassium in Ringer's solution. McCullagh and Schneider, *Ohio State M. J.*, 41: 528 (June) 1945. Three times subcutaneous dose, given sublingually, produced subcutaneous effect; five to seven times injected dose in cocoa butter ineffective by inunction. In one case, 10-30 mgm. rectally, was less effective than 6 mgm. intramuscularly given daily. Thorn et al., *J. Clin. Endocrinology*, 1: 967 (Dec.) 1941. Sublingually, 10 mgm. in propylene glycol failed to maintain health in four, previously successfully maintained by parenteral administration. Wilson, *Lancet*, 212: 762 (June) 1942. *Infrascapular insertion of pellets* Maximum in single implantation was four 150 mgm. or six 75 mgm. pellets. Five of seven were well maintained for 7-40 months. Maximum effective life of 75 mgm. pellets was ten months and average daily absorption 0.21 mgm. pellet, average number of pellets required was 4-6. Shipley, *Am. J. M. Sc.*, 207: 19 (Jan) 1941. *Intramuscularly*, 5 mgm. of hormone in sesame oil, with 1 gm. sodium chloride. After maintenance in good condition for one month, one pellet of 125 mgm. was implanted for each 0.5 mgm. hormone required by daily injection (effective 12 months). Thorn, Durrance, and Dry, *Ann. Int. Med.*, 16: 1053 (June) 1942. In 13 patients cardiac measurements kept within normal limits by following formula $Na \times D = K$ where sodium (Na) is expressed in gm., desoxycorticosterone acetate (D) in mgm., and $K = 30$ to 45 in calculating dosage of these substances. McGavack, *Am. Heart J.*, 27: 331 (Mar.) 1944.

Antagonist to Posterior Pituitary Epileptic seizures induced in epileptics, taking low mineral diet and increased water intake, by pituitrin or pitressin can be protected by desoxycorticosterone 5 mgm. daily with ordinary mixed diet and restriction of water intake lessened occurrence in two patients. McQuarrie, Anderson, and Ziegler, *J. Clin. Endocrinol.*, 2: 406 (June) 1942.

Fetal Shock in Newborn: 0.1–0.5 ml. daily gave excellent results, the most important use being in breech extraction. Berlind, Canad. M. A. J., 45: 534 (Dec.) 1941.

Insulin Coma: 10 or 20 mgm. to patients in acute coma from insulin shock improved course of coma and resulted in recovery. Aldama, Med., Madrid, 12: 703 (Oct.) 1944; through J.A.M.A., 127: 1022; 1945.

DESOXYEPHEDRINE

(d,l-N-dimethyl-phenethylamine)

Man—

Irradiation Sickness Therapy: Orally, 2.5–5 mgm. 30 minutes before breakfast, at noon and at 4 P.M. from start of x-ray sickness until three days after roentgen therapy showed definite remission in 34 of 42. Daily dose never exceeded 20 mgm. No serious side effects or evidence of habit formation (see amphetamine). Jenkinson and Brown, Am. J. Roentgenol., 51: 496 (Apr.) 1944.

DETERGENTS

Rabbits—

Local Action: Single or repeated application into eyes of 0.1% or 0.25% Aerosol "OT" (sodium di (β -ethylhexyl) sulfosuccinate), Aerosol "OS" (alkyl-aryl sulfonate), Tergitol "4" (higher secondary alcohol sulfate), Tergitol "7" (sodium acid sulfate of 3,9-diethyl-6 tridecanol), Tergitol "O 8" (sodium acid sulfate of 2-ethyl-1-hexanol) or of Duponal "M E" dry (sodium lauryl sulfate) and their single application in 0.5% concentration produced marked blepharospasm and mild conjunctival injection of 24 hour duration. 0.5% four times daily retarded epithelial regeneration. Leopold, Arch. Ophth., 34: 99 (Aug.) 1945.

DEUTERIUM

Rats—

Synthesis of Methyl Groups: Three atom per cent maintained in the body water of white rats fed a casein diet and given deuterium oxide caused deuterium to be found in the methyl groups of tissue choline. du Vigneaud et al., J. Biol. Chem., 159: 755 (Aug.) 1945.

DIAL + URETHANE

(5,5-diallylbarbituric acid)

Man—

Obstetric analgetic (1200): Intravenously, 4 ml. (dial 0.33 gm. and

urethane 1.6 gm.) given in ten minutes when cervix was 2 cm. dilated. Morphine, 8 mgm. subcutaneously one-half hour later. Van Del, J. Missouri M. A., 39: 100 (Apr.) 1912.

4,4'-DIAMIDINO-DIMETHYL STILBENE

Mice—

Trypanosoma congolense Intraperitoneally, 0.5 mgm/20 kg. cleared. Maximum tolerated dose was 1 mgm/20 kg. Fulton and Yorke, Ann. Trop. Med., 37: 152 (Dec.) 1913.

Cattle—

Trypanosoma congolense 10-12.5 mgm./kg. of 5% intravenously or intramuscularly, cleared eight of 11, three poisoned and died within 1.5 hours. Toxic symptoms: salivation, extreme dyspnea. Carmichael and Bell, Ann. Trop. Med., 37: 145 (Dec.) 1913.

4,4' DIAMIDINO-DIPHENOXY-PENTANE

Cattle—

Infected with *Trypanosoma congolense*—not effective. Doses larger than 10 mgm/kg. caused immediate poisoning. 5-15 mgm/kg. and repeated doses of 5 mgm/kg. caused delayed poisoning. 2.5 mgm/kg. produced liver injury. Daubney and Hudson, Ann. Trop. Med., 35: 175 (Dec.) 1911.

Man—

Kala Azar Therapy: 12 to 15 intramuscular injections (1.5-2 mgm/kg. each), given three times a week. Injections were painful but drug was well tolerated. Giraud and Revol, Presse med., 51: 291 (June) 1913; through Trop. Dis. Bull., 41: 109 (Feb.) 1911.

Intravenously, 1% solution in distilled water. 0.025 gm. initially, 0.05 gm. for second dose, 0.075 gm. for third, then daily increase of approximately 15-20 mgm. until 0.5 gm./kg. reached and maintained until end of therapy. 10 of 11 resistant cases and 19 of 21 ordinary cases cleared. Napier and Sen Gupta, Indian M. Gaz., 78: 177 & 201 (Apr.) 1913; through Trop. Dis. Bull., 11: 18 (Jan.) 1911.

Leishmaniasis (Indian) Average of 0.025 + 0.1793 gm. arrested ten cases. Sen Gupta, Indian M. Gaz., 79: 19 (1911).

Fatality: 0.1 gm. pentamidine (p.p. pentamethylene di-oxo) bisbenzamidine) daily for three days. An epileptoid reaction, coma and death after third injection. McComas and Martin, Lancet 216: 338 (Mar.) 1911.

4,4'-DIAMIDINO-MONOMETHYL-STILBENE DIHYDROCHLORIDE

Mice—

Trypanosomiasis: 1 mgm. intraperitoneally, protected up to ten weeks following end of drug administration. Animals inoculated 11 weeks after treatment died on the 14th day; those inoculated 12 weeks from end of treatment died on the sixth day. Other aromatic diamidines were also effective. Fulton, Ann. Trop. Med., 38: 78 (Apr.) 1944.

DIAMIDINO-STILBENE (4,4' diamidino stilbene)

Dogs—

Therapy of Tick Fever: Therapeutic dose or clinically curative dose <2.5 mgm/kg. Daubney and Hudson, Ann. Trop. Med., 35: 187 (Dec. 31) 1942.

Cattle (infected)—

Trypanosoma congolense: 20 mgm/kg. did not affect disease. Ibid., 35: 175 (Dec. 31) 1941.

Man—

Tolerated in Tuberculosis: 0.675 gm. (0.89 gm/kg.) divided into ten intravenous doses cleared leishmaniasis without extension of tuberculosis. Sen Gupta, Indian M. Gaz., 79: 49 (Feb.) 1944.

Kala Azar: Intravenously, 1 mgm/kg. increased gradually to 4 mgm/kg. at intervals of one to three days. Total amount per patient, 5.01–4.88 gm. All received two courses. Toxic reactions: breathlessness, headache, dizziness, feeling of emptiness in chest, and vomiting after first, second, or third injection. Somers, Lancet, 246. 531 (Apr.) 1944.

p,p'-DIAMINODIPHENYLSULFONE (Diasone)

Guinea Pigs—

Experimental Tuberculosis: 2.65 gm. of 1048 [disodium salt of p,p'-sulfonylbis N-acetyl α-(anilinothiomethylmercapto)-glycine] in divided doses beginning two days after infection kept animals entirely free of gross or microscopic evidence of disease, but could not be duplicated. Two other sulfone derivatives, given orally or intraperitoneally, retarded tuberculous process. Sweany, Sher, and Klock, Am. Rev. Tuberc., 53: 254 (Mar.) 1946. 400 mgm. of sulfone to 14 animals, 64% survived 228 days. 200 mgm. 4,4'-diaminodiphenylsulfone to 14 animals 71.4% survived. Only

28.6% of controls survived. Feldman and Hinshaw, Proc. Staff Meet., Mayo Clin., 20: 1611; 1915. Treatment with 300 mgm. in two divided doses daily, gave average blood concentration of 3.0 mgm per 100 ml. and 81.0 mgm. per 100 ml urine. It was most effective against acute, primary infections. No toxic or histologic changes were evident Giroux, Laval méd., 9: 788 (Dec) 1914.

Combined Action with Immunization Gross tuberculous involvement of the organs as determined by pathologic rating was 81 in control animals; 25 in those which received 0.1 gm sulfone daily for two months after infection; 47 for animals infected 33 days after immunization with 0.0005 mgm. Corper's human avirulent strain of tubercle bacillus, and 25 in immunized animals given 0.1 gm of the sulfone daily. Sher and Kloeck, Am. Rev. Tuberc, 53: 250 (Mar.) 1946.

Man—

Pulmonary Tuberculosis 30 patients were given 1 gm. daily for 120 days and were positive before and after treatment, 16 had a slight diminution of organisms. Desmeules et al., Laval med., 9: 780 (Dec.) 1914. 0.9–4.56 gm. for 120–399 days to 36 patients showed improvement in two, moderate improvement in ten, slight improvement in seven, no change in nine, retrogression in eight. Hemoglobin decreased from 6–21% in 18 patients. Blood concentrations of 0.1 mgm to 3.79 mgm per 100 ml. had no relation to dosage or degree of cyanosis Pfeiffer and Pyle, Dis. of Chest, 11: 213; 1915.

78% of 78 patients given drug over 60–275 days were definitely improved. Orally, 0.33 gm. per day for three days, then 0.66 gm. per day for three to five days and finally 1.0 gm per day, for five to six days per week. Blood concentration 1.7–2.5 mgm per cent, cerebrospinal fluid, 1.5–2.0 mgm. per cent, urine, 41.0–80.0 mgm. per cent; bronchial secretion, 0.5–1.0 mgm. per cent. *Toxic Reactions* Headache, gastric upset, palpitation, malaise, occasional visual disturbances and "blue" skin. *Pathologic changes* none in liver, spleen, kidneys, adrenals. Petter and Prenzlau, Illinois M. J., 85: 188 (Apr) 1911. Of 11, 67, 35 patients with minimal, moderate and far advanced disease who were treated with diasone, orally. 100, 91 and 71% respectively, improved. Early in study, 0.33 gm., three times per day with meals, later 1 gm. per day for three days, then 2 gm per day for three to five days (0.66 gm with each meal) finally 1 gm. per day again. Blood level over 1.5 mgm. per cent. Petter, Clin. Med., 51: 66 (Mar.) 1911.

Idiorynery: 28.67 gm. given to tuberculous patient (1 gm. daily twice,

1.33 gm. daily for 20 times) produced severe pemphigus-like reaction three weeks later. Pfuetz and Pyle, J.A.M.A., 125: 354 (June 3) 1944.

Toxicity: Orally, up to 3.0 gm/24 hours of sulfone showed no toxicity. Feldman and Hinshaw, Proc. Staff Meet., Mayo Clin., 20: 1611; 1945.

Toxic Reactions: Dermatitis, fever, malaise and systemic disturbances and in a few, secondary anemia, kidney damage and mental depression. See Pfuetze and Pyle, 1945.

Leprosy: Orally, 0.3 gm. daily in divided doses during meals, increased to 0.6 gm. a day after one to two weeks, and to 1 gm. per day several weeks later controlled the disease in 44 of 47. Improvement took place after four months. Faget and Pogge, New Orleans M. & S. J., 98: 145 (Oct.) 1945.

' DIBUTOLINE

(dimethyl-ethyl- β -hydroxyethyl-ammonium-sulfate-di-n.
butyl-carbamate)

Rats—

Toxicity: LD₅₀: 22 mgm/kg. intraperitoneally; 15 mgm/kg. caused respiratory distress. Orally, 500 mgm/kg. produced no toxic reaction. Featherstone and White, J. Pharmacol. & Exper. Therap., 84: 105 (June) 1945.

Dogs—

Effect: Subcutaneously, 0.25 mgm/kg. caused colonic relaxation for 90 minutes, relaxation of the small intestine for 70 minutes and gastric relaxation; a slight depression in pulse rate for five minutes, then a rise of 16–30 beats per minute, reaching normal in 30 minutes; had no significant effect on urinary bladder function, but overcome effect of 0.5 mgm. mecholyl/kg. Orally, 50 mgm/kg. relaxed stomach and gut, but 10 mgm/kg. orally or 5 mgm/kg. locally had no effect on the small intestine. Intravenously, 2 mgm/kg. increased blood pressure slightly. Ibid.

ORTHO-DICHLOROBENZENE

Mice—

Toxicity: Exposure to atmosphere saturated with the compound—mice became excited and died next day. Riedel, Arch. f. Gewerbepath. u. Gewerbehyg., 10: 546; 1941.

Rats—

Toxicity: Died after abdomen painted. Ibid.

Dogs—

Exposure to 2 ml. in atmosphere for two hours daily for two weeks showed no abnormal effects Ibid.

6,7-DICHLORO-9-d-RIBOFLAVIN**Bacteria—**

Growth Inhibition: Concentration of 10^{-8} gm/ml. inhibited growth of *Staphylococcus aureus*, *Streptococcus plantarum* and two strains of lactic acid bacteria but not yeast. Kuhn, Weygand, and Möller, Ber., 76B: 1044 (Oct.) 1943.

DICHLOROMETHANE**Rats—**

Running Activity: 5,000 parts per million in air definitely diminished activity (standard type revolving drum used) although no depressant effects were observed Heppel and Neal, J. Indust. Hyg. & Toxicol., 26: 17 (Jan.) 1944.

DICHLOROPHENARSINE HYDROCHLORIDE

(Clorarsen)

(Phenarsine hydrochloride)

Man—**DICOUMARIN; DICUMAROL****Rats—**

Conversion to Salicylate Disproved 25 mgm/day for three days fed to rats excreted no salicylates, given 25 mgm sodium salicylate/day excreted 21.0 mgm. *Prothrombin time* with salicylate, control and dicumarol was 27.2 seconds, 32.1 seconds, and over five minutes, respectively. Lester, J. Biol. Chem., 154: 305 (June) 1944.

Rabbits—

Platelet Adhesiveness: Intravenously, 0.05 mgm/kg or orally 1 mgm. per kg for seven days resulted in a doubling of the prothrombin time and diminishing of the adhesiveness of blood platelets. Wright, J. Path. & Bact., 57: 382 (July) 1945.

Toxicity. Intravenously, 1-2 mgm/kg daily—fatal in ten days to all. With 0.1-0.5 mgm/kg ~3/15 died on 29th day. Hemorrhage and pulmonary edema were observed Rose, Harris, and Chen, Proc. Soc. Exper. Biol. & Med., 50: 228, 1942.

Dogs—

Experimental Thrombosis: Orally, 5 mgm., two days later 0.25 ml. monoethanol amine oleate (monolate) was injected into radial veins. Veins removed six to nine days later and histologic examination made. Only two (6.6%) from dicumarol treatment showed definite thrombi, four others (13.3%) showed possible thrombi, while 15 (50%) of controls were definitely thrombosed and two (6.6%) had possible thrombi. Thill et al., Proc. Soc. Exper. Biol. & Med., 54: 333 (Dec.) 1943. Single intravenous doses of 10 mgm/kg. increased prothrombin time and prevented formation of intra- and extravascular thrombi after mechanical trauma. Dose tolerated without apparent discomfort. *Reaction:* Marked vasodilatation of capillaries, small arteries and veins. Dale and Jaques, Canad. M. A. J., 46: 546 (June) 1942.

Orally, 10–25 mgm. for three to five days resulted in rapid increase in prothrombin and coagulation time and prevention of thrombus formation. Richards and Cortell, Proc. Soc. Exper. Biol. & Med., 50: 237 (June) 1942.

Toxicity: 50, 20, 10, and 5 mgm/kg. caused death in all 21 dogs in 28 days. Hemorrhage in various tissues and organs and pulmonary edema. Rose, Harris, and Chen, Proc. Soc. Exper. Biol. & Med., 50: 228; (June) 1942.

Man—

Effective Intravenous Dose: 4 mgm/kg. of disodium salt.

Effective Oral Dose: 5 mgm/kg. of free acid initially, followed by 1.5 mgm/kg. daily. Meyer, Bingham, and Axelrod, Am. J. M. Sc., 204: 11 (July) 1942.

Rectal Administration: 3 mgm/kg. rectally in patient with thrombosis of the right postero-inferior cerebellar artery, or 5.0 mgm/kg. incorporated in cocoa butter suppositories were effective. In other cases, 5, 7, 10 mgm/kg. doses were occasionally effective. Meyer and Spooner, Proc. Soc. Exper. Biol. & Med., 54: 88 (Oct.) 1943.

Therapeutic Dose: 300 mgm. initially, followed by 200 mgm. next morning. Follow-up doses of 200 mgm. usually achieved desired prothrombin level of 60–30% of normal. Follow-up doses increased to 300 mgm. or more in dicumarol resistant and reduced to 100 mgm. in susceptible persons. Zucker, J.A.M.A., 124: 217; 1944.

Hypoprothrombinemia: Produced by oral administration of two to three doses of 125 mgm. after meals, taking effect in eight to ten hours

with almost no untoward effects. Von Kaulla, *Klin. Wchnschr.*, 22: 205 (Mar.) 1943; through *Quart. Rev. Med.*, 1: 158 (Feb.) 1944.

Uncontrollable Hemorrhage: Orally, 300 mgm/day was administered for 21 days. Generalized arteriosclerosis, hemorrhage of meninges, skin, retroperitoneal tissues, kidneys, urinary bladder, stomach and duodenum were observed. Shlevin and Lederer, *Ann. Int. Med.*, 21: 332 (Aug.) 1944.

Cerebrovascular Diseases: 300 mgm. for two days was not repeated until prothrombin time had returned to 35 seconds. Rapid improvement with cerebral thrombosis. Multiple sclerosis not benefited. Should be used with caution in patient taking large amount of salicylates, e.g., aspirin; with ulcerating or granulating wounds, in febrile states and during menstruation Young, *Quart. Rev. Med.*, 2: 188 (Feb.) 1945.

Intravascular Thrombosis 300 mgm. first day, 200 mgm. second day and 0-200 mgm. thereafter, depending on prothrombin time. Blood prothrombin must be 25-50% of normal based on prothrombin time before drug has effect. Ekstam, *Minnesota Med.*, 27: 455 (June) 1944.

Postoperative Thrombosis Recommended dose of 300 mgm. first day and 200 mgm. daily thereafter until prothrombin time is less than 20% of normal. 60 mgm. menadione bisulfite given intravenously if excessive prothrombin deficiency and bleeding occurred. **Contraindicated:** In purpura, blood dyscrasias, subacute bacterial endocarditis **Indicated:** In thrombophlebitis, lung infarction, embolism, predisposition to thrombosis or embolism. Allen, *Clin. Med.*, 52: 166 (May) 1945.

Prevented with maintenance dose of 100 mgm. daily and total dose varied from 700 to 800 mgm in 102 cases. Reich, Yahr and Eggers, *Surgery*, 18: 238 (Aug.) 1945.

Thrombophlebitis Treatment: 300 mgm first day, 200 mgm. second, and 50-200 mgm. daily thereafter in accordance with prothrombin level. Yahr, Reich, and Eggers, *Surg., Gynec. & Obst.*, 80: 615 (June) 1945. 300 mgm. for patient over 7 kg followed by 100 mgm daily until prothrombin fell to 50-60%. Evans, *Connecticut M. J.*, 8: 71 (Feb.) 1944. 300 mgm. on first day, 200 mgm. on second with 0-200 mgm doses depending on prothrombin time. Length of treatment was 17 days. Glueck, *Ohio State M. J.*, 41: 714 (Aug.) 1945.

Thrombophlebitis and Pulmonary Embolism Heparin was given intravenously immediately on diagnosis, when clotting time was raised from 20-25 minutes, initial oral dose 5 mgm/kg of dicoumarin was given and heparin was discontinued 36 hours later. 1.5-3 mgm/kg., dicoumarin were administered daily over following two to three weeks. Greatest potential danger is cumulative effect. Evans, *Lahey Clinic Bull.*,

2:248 (Apr.) 1942. Orally, 300 mgm. on third postoperative day and on every day thereafter when prothrombin time was below 35 seconds caused only two thromboses and no fatal emboli occurred among 624 patients. Barker, Minnesota Med., 27: 102 (Feb.) 1944.

Thrombophlebitis and Emboli: 300 mgm. initially followed by 100 to 200 mgm. every two hours was usually adequate, although varying responses required daily prothrombin determination (14 with thrombophlebitis were controlled and two with pulmonary embolus were relieved). Nelson, J. Kansas M. Soc., 46: 325 (Oct.) 1945.

Pulmonary Embolism prevented with 300 mgm. given orally day before operation to patient with previous attack of embolism; 200 mgm. per day thereafter, maintaining prothrombin time at 35-45 seconds until eighth postoperative day. Flinn, Arizona Med., 1: 20, 24 (Jan.-Feb.) 1944.

Puerperal Thrombosis: Therapy of 300 mgm. daily. Bleeding and clotting time checked to prevent overdosage. Administered with no untoward effects. Davis and Porter, Brit. M. J., I: 718 (May) 1944.

Trauma and Gangrene: Orally, 300 mgm. caused prothrombin clotting time to remain elevated for nine days when uremia was present but with improvement clotting time returned to normal. Clotting time for undiluted plasma was maintained at 30-35 seconds to prevent overdosage. Brambel and Loker, Arch. Surg., 48: 1 (Jan.) 1944.

DIENOESTROL

(γ -di-p-hydroxyphenyl- Δ^8 - γ hexadiene)

Man—

Menopause. Orally, 0.1 mgm. twice per day relieved or arrested hot flashes in seven of eleven patients Barnes, Brit. M. J., I: 79 (Jan.) 1944.

DI-(2-ETHYLHEXYL) PHTHALATE

Rats—

Acute Toxicity: LD₅₀ Orally, 30.6 gm/kg.; intraperitoneally, 30.7 gm/kg. *Chronic Toxicity:* Orally, 0.9 gm. or more per kg. for 90 days caused testicular injury. 0.4 gm. or less caused little injury. Shaffer, Carpenter, and Smyth, J. Indust. Hyg. & Toxicol., 27: 130 (May) 1945.

Rabbits—

Acute Toxicity: LD₅₀. orally, 33.9 gm/kg. *Absorption:* Application of 20 ml/kg. to intact rabbit skin killed two of six animals in 24 hours. Non-irritating to eye or skin. Ibid.

Man—

Excretion: 4.5% of ten and five gm respectively was recovered in urine in 24 hours. Ibid.

DIETHYLSTILBESTROL

Chicks—

Oviduct. Subcutaneously, 0.5 mgm. in 0.1 ml. corn oil, daily for six days increased weight 40 to 50 fold. Hertz, *Endocrinology*, 37: 1 (July) 1945.

Chickens (Single Comb White Leghorn Females)—

Genital Tract: Growth to 48 times normal with 11 doses of 0.5 mgm. injected intramuscularly Herrick, *Poultry Sci.*, 23: 65 (Jan.) 1944.

Cockerels—

Feeding Effect: 1 mgm or more per day for periods up to 12 weeks improved market grade of birds. No advantage in continuing beyond six weeks; and age had no noticeable effect. Sykes, Davidson, and Barrett, *Poultry Sci.*, 24: 542 (Nov) 1945.

Mice—

Pregnancy: Subcutaneously, 0.005 to 1.0 mgm in sesame oil daily developed and accelerated tubal passage of fertilized ova and pregnancy was terminated. Burdick and Vedder, *Endocrinology*, 28: 629, 1941.

Mice (Strain C3H)—

Carcinogenic Effect (in male) 4.35 to 14.5 mgm. administered during 24 to 27 weeks developed breast tumors. Shimkin and Grady, *J. Nat. Cancer Inst.*, 2: 55; 1941.

Mammary Tumor formed by implanting subcutaneously, 1.6 mgm. pellets containing 25% diethylstilbestrol in cholesterol in mice fed on low cystine diet. White and White, *J. Nat. Cancer Inst.*, 4: 413 (Feb.) 1941.

Rats (Castrated Normal Male and Female)—

Carbohydrate Metabolism Subcutaneously, 100 gammas daily for 20 days increased liver glycogen and blood sugar. Janes and Nelson, *Am. J. Physiol.*, 136: 136 (Mar.) 1942.

Rats—

Cholesterol. Within 24 hours after single subcutaneous injection of 0.5 mgm. per 0.1 ml. sesame oil, there was cholesterol in adrenals. 0.5 mgm. daily reduced serum cholesterol values. Levin, *Endocrinology*, 37: 31 (July) 1945.

Growth Retardation. 2 mgm daily caused definite drop in weight which was restored by daily injection of 0.5 ml. pituitary growth hor-

mone for ten days. Richards and Kueter, *Am. J. Physiol.*, 133: 423 (June) 1941.

Toxicology: Loss of weight in all by oral diethylstilbestrol, its dipropionate, its monomethyl ester, its monomethyl ether acetate, hexestrol and its monomethyl ether in very high doses. Daily doses in mgm/kg. were 0.001 to 100, 20, 5, 1.0, 20, and 10 respectively. Duration of treatment was from two to four weeks. Teague, *J. Pharmacol. & Exper. Therap.*, 75: 145 (June) 1942.

Hamsters—

Pituitary Cellular Proliferation: Caused in intermediate lobe by treatment with 10 mgm., subcutaneously over a prolonged period; not malignant. Vasquez-Lopez, *J. Path. & Bact.*, 56: 1 (Jan.) 1944.

Rabbits—

Breeding: Intramuscularly, 0.5 ml. increased sexual receptivity; resulted in successful mating. Hutson, *J. Am. Vet. M. A.*, 107: 143 (Sept.) 1945.

Metabolism: Intramuscularly, 3 gm. in divided doses was given over 14 days. Stilbestrol monoglycuronide, 1.5 gm. was isolated from urine, indicating conjugation with glucuronic acid was mechanism in intermediary metabolism. Mazur and Shorr, *J. Biol. Chem.*, 144: 283 (June) 1942.

Thyroid Gland: 1 mgm., injected daily caused complete inhibition of ovarian activity for 30 days, which was ineffective in thyroidectomized animals. Chu and You, *J. Endocrinol.*, 4: 115 (Jan.) 1945.

Dogs—

Blood Picture: Five mgm. daily caused anemia in one to three weeks. One mgm. had no effect. Large doses resulted in fall of red blood cells, reticulocytes, thrombocytes, and granulocytopenia. Hemorrhages in organs observed. Tyslowitz and Dengemanse, *Endocrinology*, 29: 817 (Nov.) 1941.

Galactose Absorption: Five to 10 mgm. in oil daily, injected for 22 days increased rate of galactose absorption from intestinal tract of eight dogs. Grauer, Starkey, and Saier, *Endocrinology*, 30: 474 (Mar.) 1942.

Hair Loss in male animals: 330 mgm. in 129 days, 1790 mgm. in 292 days, 1850 mgm. in 280 days and 2985 mgm. in 291 days respectively to four dogs showed loss of hair corresponding to amount of hormone. Mulligan, *Proc. Soc. Exper. Biol. & Med.*, 54: 21 (Oct.) 1943.

Acute Prostatitis: Intramuscularly, 6 mgm. followed by 4 mgm. for three days. Sulfathiazole was also given. Complete regression Kendall, *Vet. Med.*, 40: 387 (Nov.) 1945.

Heifers—

Lactation: Induced by subcutaneous implantation of small tablets, totaling 2.5 or 5.0 gm. Folley and Malforess, *J. Endocrinol.*, 4: 1 (July) 1944.

Man—

Amenorrhea (secondary) One mgm. per day 35 times plus 10 mgm. progesterone per day for five doses usually produced bleeding within two to five days. Starting on fourth day of bleeding, therapy repeated with 0.5 mgm. stilbestrol, and then 0.3 mgm. with progesterone omitted. Smith, *New England J. Med.*, 230: 339 (Mar.) 1944.

Bleeding Hazard: Daily dose, not exceeding 0.1 to 0.5 mgm. was given for pronounced menopausal vasomotor symptoms, since drug produced postmenopausal bleeding. Novak, *J. A. M. A.*, 125: 98; 1944.

Breast Cancer: 0.5 mgm. daily for three periods of 24 days caused disappearance of spheroid cell carcinoma. Edwards, *Brit. M. J.* II: 659 (Nov.) 1943. 1.0 to 5 gm. daily for varying periods up to 24 weeks effected improvement in 27 of 68 patients over 60 years of age. Ellis et al., *Proc. Roy. Soc. Med.*, 37: 731 (Oct.) 1944.

Breast Engorgement Prevention Orally, 10 mgm. after meals on day of delivery and 5 mgm. daily thereafter until 25 mgm. was given. Or, 5 mgm. three times a day for the first two days and 5 mgm. daily for ten to 12 days. Bulowe, *Yale J. Biol. & Med.*, 14: 631 (July) 1912. Orally or intramuscularly, 10 to 15 mgm. followed by 5.0 to 10 mgm. on two succeeding days. Rutherford, *West J. Surg.*, 50: 282 (July) 1912.

Carcinoma of Prostate Five mgm. daily, was given for two to three weeks initially; maintenance dose was 2 to 3 mgm. daily. Not curative but death was postponed. Millen, *Proc. Roy. Soc. Med.*, 37: 357 (May) 1914. Three hundred forty-two cases in literature reviewed. Estrogenic therapy was most effective and preferred to castration. 5 mgm. in oil intramuscularly daily for 40 days followed by 5 mgm. three times a week until prostate was considered clinically normal. Kahle and Beacham, *Urol. & Cutan. Rev.*, 48: 1 (Jan.) 1914. Treated with varying doses in oil, intramuscularly. One patient received 503 mgm. (12,575,000 international units) in 1.0 to 5 mgm. doses during 16 months. Prompt relief of pain and urinary symptoms and general improvement in health were observed. Kahle, Ogden, and Getzoff, *J. Urol.*, 48: 83 (July) 1912. Intramuscularly, 10 mgm. daily for five to ten days, then 1 mgm. orally two to three times daily for two months gave satisfactory results in eight cases of inoperable carcinoma of prostate. Chute and Willets, *New England J. Med.*, 227: 863 (Dec.) 1912. Two to 5 mgm. initially, then gradually reduced

and maintained on 1.0 to 2 mgm. twice a day markedly improved 20 patients. Ferguson, *Clinical Proceedings*, Cape Town (Apr.) 1945; through *Urol. & Cutan. Rev.*, 49: 628 (Oct.) 1945. Initial dose was 1 mgm. three times a day, increased by 1.0 mgm. per dose up to 5 mgm. three times a day or four times a day, then reduced as indicated by serum acid phosphatase level. Maintenance dose was 1.0 to 10 mgm. per day. Riches, *Biochem. J.*, 39: v, 1945. Three mgm. daily up to 12 mgm. Heckel and Kretschmer, *J.A.M.A.*, 119: 1087; 1942. Subcutaneously, 1.0 mgm. increased to 5 mgm. or more until symptoms were entirely controlled. Dodds, *Proc. Roy. Soc. Med.*, 37: 353 (May) 1944. Initial dose of 2 mgm., two or three times daily increased to 10 to 15 mgm. daily. Intramuscularly, 25 mgm. testosterone propionate for 15 days increased blood acid phosphatase if lesion was malignant. Wray, *Lancet*, 248: 783 (June) 1945.

Cancer of Bladder and Uterus controlled by 10 mgm. plus radiation therapy. Herbst, *J.A.M.A.*, 127: 57; 1945.

Desensitization to nausea and vomiting from stilbestrol. Parenteral: intramuscularly or subcutaneously, in oil every second and third day, gradually increased by 0.05 to 0.1 mgm., each dose until 1.0 mgm. was reached without reaction. Then enteric coated tablets of 0.5 to 1 mgm. were given daily. Orally: 0.1 mgm. tablets once daily for five days, then increasing dose by 0.05 to 0.15 mgm. every five to six days until therapeutic level required was reached. Finch, *J.A.M.A.*, 119: 400; 1942.

Dysmenorrhea: Suppositories, containing 0.4 to 0.8 mgm. estradiol or 0.2 to 0.5 mgm. stilbestrol used nightly for 14 to 18 days in intramenstrual period relieved 60%. Greenblatt, *J. South Carolina M. A.*, 38: 62 (Mar.) 1942. Orally, 5 mgm. per day for 20 days, starting at end of menstrual flow, completely relieved or improved 31 of 70. Patton, *Am. J. Obst. & Gynec.*, 50: 417 (Oct.) 1945. 0.5 mgm. given per day or twice a day. Weinstein, *New Orleans M. & S. J.*, 96: 396 (Mar.) 1944.

Essential Dysmenorrhea. Orally, 1.0 to 2 mgm. daily for 10 to 24 days. For desired results treatment was begun seven days before ovulation or menstruation. Sturgis, *New England J. Med.*, 226: 371 (Mar.) 1942.

Gonococcus Vaginitis in Children: Vaginal insertion of 0.1 mgm. in suppository form every night was treatment of choice. Orally, 1 mgm. daily. Breast enlargement resulted in both treatments. Woodruff and Te Linde, *South. M. J.*, 35: 389 (Apr.) 1942.

Pseudo-hermaphroditism: Orally, 5 mgm. daily for four months accentuated female secondary sex characteristics in a five year old patient. Reduction to 3 mgm. because of toxicity and continued for four months.

Further reduction to 2 mgm daily. After six months, clitoris had decreased. McIntosh and Brown, J. Pediat., 27: 323 (Oct.) 1945.

Hypergonadism: 1.0 mgm. every other day for ten days followed by 1.0 mgm. daily until 30 mgm. was given had beneficial effect. Foote, J. Nerv. & Ment. Dis., 99: 928 (June) 1944.

Hypersexual Males: 300 to 600 mgm. caused loss of libido and produced degenerative changes in seminiferous tubules. Connelly, J. Michigan M. Soc., 44: 377 (Apr.) 1945.

Lactation, prevention and suppression: Orally, 5 mgm. twice a day to post-partum women. Douglas, Wanless, and Deeds, Ohio State M. J., 38: 452 (May) 1942.

Lactation Suppression: Total of 30 to 45 mgm. was given in 5 mgm. doses orally three times a day. Bloom, Am. J. Surg., 54: 443; 1941. Ten mgm. was given on day of delivery, followed by 5 mgm. daily for next ten days and then 1.0 mgm. daily for next 20 days for a total of 80 mgm. in one month. Paradis, Laval méd., 10: 344 (May) 1945. Orally, 10 mgm. daily for four days. Diddle, Nagyfy, and Sells, J. Clin. Endocrinol., 2: 307 (May) 1942.

Menopause Therapy. 20 to 30 mgm. per day orally, for one to six months for a total dosage of 120 to 180 mgm. Karnaky and Rathbarn, Am. J. Surg., 56: 636 (June) 1942. Vulva-pruritis were treated with 10 mgm. daily. Arenas, Ann. brasil. de gynec., 12: 441 (Dec.) 1941; through J.A.M.A., 118: 1417; 1942.

Pre-natal Use: 10 mgm. daily from first month pregnancy to a total of 18 gm. caused no ill effects. In non-pregnant women, hyperthyroidism was simulated by liver during pregnancy as compared to control. In non-pregnant women. One to 25 mgm daily or every other day for one to eight months produced no systemic changes in children. Karnaky, J. Clin Endocrinol., 5: 279; 1945.

Pregnancy Complications: Initially, 5 mgm., increased every night by 5 mgm. until nausea was relieved in gastrointestinal symptoms. 10 mgm. at bedtime with tolerance doses of thyroid during first trimester were successfully used to prevent miscarriage in pregnancy with retroverted uterus. Imminent miscarriage was treated with 25 to 50 mgm. every 15 minutes until cessation of cramping and bleeding, then 10 mgm. every hour for six doses, finally 10 mgm per day plus thyroid plus vitamins C and K. Hudgins, West Virginia M. J., 40: 75 (Mar.) 1941.

Prostatic Hyperplasia Intramuscularly, 1 mgm. of dipropionate in

oil for six injections. Colon, Bol. Asoc. méd. de Puerto Rico, 34: 41 (Feb.) 1942; through J.A.M.A., 119: 682; 1942.

Scalp Ringworm: Orally, 0.25 mgm. per day checked spread of disease and 0.5 mgm. a day for three weeks eradicated ringworm in three children aged 6.5 to 7.5 years. Law, M. Press., 1: 351 (June) 1943.

Toxicity: Chronic arthritis was treated with maximum doses of 1.0 to 3 mgm. daily for five to nine weeks, total of 55 to 189 mgm. in 20 women and ten men. Marked improvement was observed in 80%; nausea in 50% was controlled by dose reduction. There was no evidence of liver damage, no significant change in blood count, urinalysis, blood urea, and blood glucose. Aaron et al., Am. J. Digest. Dis. & Nutrition, 8: 437 (Nov.) 1941.

Functional Uterine Bleeding: Five to 10 mgm. for 15 consecutive days starting during excessive bleeding, followed after next normal menstrual cycle by 2 to 3 mgm. from 10th to 13th day of cycle and then 10 mgm. anhydro-hydroxyprogesterone daily for ten days starting on 14th day of cycle. McGinn, J. Clin. Endocrinol., 2: 302 (May) 1942.

Dysfunctional Uterine Bleeding: For severe or prolonged bleeding, 10 to 50 mgm. injected into anterior wall of cervix or orally every 15 minutes for three to 24 hours until bleeding stopped. 5 to 10 mgm. should be given at 9 P.M. for 30 to 40 days. Karnaky, J. Clin. Endocrinol., 3: 648 (Dec.) 1943.

Vulvovaginitis: 1.0 mgm. three times a day until 20 mgm. was administered arrested over 90% of cases. Russ, Collins and Powell, J. Clin. Endocrinol., 2: 383 (June) 1942.

DIETHYLSTILBESTROL DIPALMITATE

Man—

Menopause: Diethylstilbestrol dipalmitate was found superior to diethyl stilbestrol and diethyl stilbestrol dipropionate for parenteral therapy. With amounts up to 5 mgm. of diethyl stilbestrol relief was obtained on an average of nine to ten weeks with dipalmitate, four weeks with diethyl stilbestrol, and five weeks with dipropionate. Freed, Eisin, and Greenhill, J.A.M.A., 119: 1412; 1942.

DIETHYLSTILBESTROL ETHERS

Rats (spayed)—

Estrogenic Potencies. 60% estrus was produced with 3 gammas stilbestrol, 15 gammas dimethyl ether, 30 gammas diethyl ether. 25% estrus was produced with 100 gammas dipropyl ether. Sondern et al., Endocrinology, 28: 849, 1941.

DIGITALIS

Chick Heart—

Bioassay: Based on ability of digitalis to produce auricular ventricular block in embryonic chick heart. Lehman and Paff, J. Pharmacol. & Exper. Therap., 75: 207 (July) 1912.

Frogs—

Assay Method: Data for construction of composite dosage-response curves for digitalis and ouabain (*Strophanthus gratus*) presented. Allmack and Morrell, J. Am. Pharm. A. (Scient. Ed.), 30: 1 (Jan.) 1911.

Cats—

Assay Method. (276 estimations using 1000 cats) De Lind Van Wynaerden procedure, using three cats, gave results within 10% in 95% of cases. Esvald, Arch. internat. de pharmacodyn. et de therap., 65: 216 (Feb. 1) 1911.

Comparison of Potency Digitalis specimens, found weak by frog method were full strength when administered to man. Intensity of action corresponded to number of cat units Gold, Cattell, et al., J. Pharmacol. & Exper. Therap., 73: 212 (Oct.) 1911.

Status of Bioassay with experimental evidence U.S.P. frog method potency ($\pm 20\%$) tested by cat method showed potency range of 0.35–0.96. Three cat units of digitalin produced same effects as 20 cat units of digitalis. Gold and Cattell, Science, 93: 197 (Feb. 28) 1911.

Dogs—

Large Dose Effect: 1–1.33 cat units per kg. body weight produced in 10 dogs bradycardia, partial or complete auriculoventricular heart block and ectopic impulses of ventricular origin. These changes were abolished by no more than 1 ml. of 10% alcohol solution of pentobarbital per 2.3 kg. in five dogs. Ven Dellen, Roberts, and Miller, Am. Heart J., 23: 772 (June) 1912.

Man—

Arteriosclerotic Heart Failure: Not more than 0.20–0.30 gm. (3–4.5 gr.) of U.S.P. XI digitalis for the first two days. Mortality of those with normal rate was 6.4%, those with sinus tachycardia, 60%; therefore action is on myocardium. Most effective on those with isolated failure of left ventricle and normal rate and least effective on combined ventricular failure and sinus tachycardia (Mortality 76%) Flaxman, J.A.M.A., 119: 252, 1912.

Assay by Electrocardiographic Changes: Subjects were ambulant and had essentially normal electrocardiograms with fairly constant control

tracings, sensitive to 22% difference in dosage. Calibration was effected by three doses of U.S.P. Reference Digitalis Powder, differing from each other by 22%, given at intervals of four weeks. Electrocardiograms were taken immediately before and 24 hours after each dose. The unknown preparation was then selected at a dose calculated to act within the calibrated range, but not coinciding with the two extremes. Ratio of dose of unknown to dose of standard represented the relative potency of the two preparations in one subject. The average of these ratios for six or more patients established the potency of unknown in relation to standard. Gold et al., *J. Pharmacol. & Exper. Therap.*, 75: 196 (July) 1942.

Auricular Fibrillation: Recurrent cardiac failure was prevented with a maintenance dose of 0.1-0.2 gm. daily of powdered digitalis leaves after digitalization. Sokolow et al., *Ann. Int. Med.*, 16: 427 (Mar.) 1942.

Auricular Flutter: 0.2 gm. every four hours for 24-36 hours was considered as a better drug. If digitalis or quinidine was not effective, 1.0 gm. quinidine sulfate in 500 ml. saline was given slowly. Bloom, Hoffman, and Hoover, *South. M. J.*, 36: 804 (Dec.) 1943.

Digitalizing Doses: 1.5 gm. powdered digitalis U.S.P. X for 50 kg. patients; 1.0 gm. U.S.P. XI or 1.25 gm. U.S.P. XII were needed. Freedberg and Blumgart, *New England J. Med.*, 227: 874 (Dec.) 1942.

Normal Sinus Mechanism: Occurred in auricular fibrillation without congestive heart failure following digitalization with total of 1.75 gm. and 1.55 gm. in two cases, respectively, given over six days. Movitt, *J.A.M.A.*, 124: 1240; 1944.

Coagulation Time: Average time was 9.45 and 9.50 minutes respectively, before and after digitalization in ten cases of heart failure. Sokoloff and Ferrer, *Proc. Soc. Exper. Biol. & Med.*, 59: 309 (June) 1945.

Rhythm: After a full therapeutic dose, those with normal cardiac rhythm showed average decrease of 12 beats per minute and in patients with cardiac disease a decrease of 12 beats, the minimum being reached four days after massive dose and eight days after the usual slow method. Lyon, *Edinburgh M. J.*, 50: 746 (Dec.) 1943.

Auriculoventricular Block (six cases): One patient received 0.05-2.0 gm. powdered digitalis leaf daily and occasionally mercurophylline intravenously; discontinued when Adams-Stokes attacks occurred for a few days, and resumed in lower doses. Intramuscularly, 0.35 mgm. strophanthin-K did not alter rhythm but 0.03-0.09 gm. daily for three weeks increased arrhythmia. Winternitz and Langendorf, *Am. Heart J.*, 27: 301 (Mar.) 1941.

Clotting Mechanism. Average decrease of 3.3 minutes in clotting time

of all (24) patients during digitalization Gilbert et al., Central Soc. for Clinical Research, through J.A M A , 124 736, 1944.

Digitalization: Single dose of 0.85 gm decreased heart rate about 30% in four to ten hours. Katz and Wise, Am. Heart J , 30. 125 (Aug.) 1945.

DIGITALIS DERIVATIVE

(Cedilanid)

Man—

Digitalizing Dose: 8 ml. intravenously, 6–14 ml. in 24 hours in divided doses digitalized almost all patients Maintenance dose was 1–3 ml. intravenously each day. Sokolow and Chamberlain, Am. Heart J., 23: 213 (Feb.) 1942.

Oral: 6–7.5 mgm. in 72 hours; maintenance dose was 1.6 mgm. Chamberlain and Sokolow, Am. Heart J . 23 213 (Feb.) 1942.

DIGITALIS DERIVATIVE

(Digilanid)

Man—

Maintenance Dose 0.333 mgm. in 70% of cases. Sieve, M. Ann. District of Columbia, 11: 47 (Feb) 1942.

DIGITALIS DERIVATIVE

(Lanatoside C)

Cats—

Mean Lethal Dose 0.261 mgm/kg, given intravenously. De Graff and Lehman, Proc. Soc Exper Biol. & Med., 45 323, 1940

Dogs—

Daily Intravenous Injection 0.2–0.5 cat unit/kg. for 16–33 days showed diffuse and widespread damage of heart muscle. LaDue, Proc. Soc. Exper. Biol & Med , 46. 651 (Apr.) 1941

Effect on Myocardium Intravenously, 0.108 mgm/kg. for 21–91 days caused slight myocardial abnormalities in six of eight dogs. Rosenblum, Biskind and Kruger, Am Heart J., 21. 731 (Dec.) 1942.

Extrasystoles. Subapical injection of 0.03 mgm. caused extrasystoles with fixed coupling or short paroxysmal tachycardia in 19 dogs. Scherf, Exper. Med. Surg., 2 70 (Feb.) 1941.

Man—

Cardiac Cases Average oral dose 0.5–1.5 mgm Auricular fibrillation, normal sinus rhythm, auricular flutter due to hypertension, arterio-

sclerosis and rheumatism therapy. Scholder, New York State J. Med., 45: 78 (Jan.) 1945. Biologic standardization eliminated; intravenous medication was potent and dependable and more rapid absorption and elimination minimized risk of cumulative effect. Ibid.

Arrhythmias: Intravenously, 1.6 mgm. to eight patients re-established normal sinus rhythm within 48 hours. Immediate after effect, primary ventricular slowing. Tandowsky, Am. Heart J., 29: 71 (Jan.) 1945.

Congestive Heart Failure: Intravenously, 0.8 to 1.6 mgm. lowered abnormal venous pressure and circulation time fell to normal levels within two to six days. Maintenance doses of 0.1 to 0.3 gm. digitalis folia started six to 12 hours after injection of cardiac glycoside. Suggested therapeutic dose was 0.4–0.8 mgm. intravenously for congestive heart failure in digitalized patients. Ray and LaDue, Am. Heart J., 30: 335 (Oct.) 1945.

DIGITONIN

Cats—

Enterol Resorption of Strophanthidin: 0.5, 1.5, 3.0, 5.0, and 10.0 mgm/kg., and the highest resorption after Magnus-Hatcher dose/kg. of *strophanthidin* followed a 3 mgm/kg. dose of digitonin. The relation of g-strophanthidin to digitonin was 1:30. After 5 and 10 mgm/kg. doses of digitonin, the resorption of g-strophanthidin decreased. Svec, Arch. f. exper. Path. u. Pharmacol., 195: 233; 1944.

DIGITOXIN

Cats—

Toxicity: MLD in cats anesthetized with sodium pentobarbital or a combination of urethane and chloralose, 0.474–0.507 mgm/kg. 20% decrease in sinus rate by injection; 30% of fatal dose infusion caused slowing of heart rate; infusion with 75% of fatal dose caused irregularity of heart beat. (See ouabain.) Krueger and Unna, J. Pharmacol. & Exper. Therap., 76: 282 (Nov.) 1942.

Dogs—

Myocardial Necrosis: By 0.150 mgm/kg., 7–12 injections in two dogs. Rosenblum, Biskind, and Kruger, Am. Heart J., 24: 734 (Dec.) 1942.

Extrasystoles: Caused by subapical injection 0.1% solution and persisted for 45 minutes. Scherf, Exper. Med. & Surg., 2: 70 (Feb.) 1944.

Man—

Digitalization: Single oral dose safely digitalized a patient in a few hours, 1.2 mgm. (3 cat units). Completely absorbed from gut; nausea

occurred in one of 50 Gold et al, J.A.M.A., 119 928, 1942. Orally 1.2 mgm. (may be given intravenously) initially, followed by 0.2 mgm. daily thereafter provided and maintained satisfactory digitalization in six to ten hours. Other preparations required 36 to 72 hours for digitalization. 1.2 to 1.5 mgm. produced the same effect as 1 2 to 1 5 gm digitalis without gastric irritation, nausea or vomiting. Gold, New York Med, (No 19) 1: 178 (Oct.) 1945. Single dose of 1 2 mgm was satisfactory in patient with chronic auricular fibrillation Heart rate decreased 30% in four to ten hours. Intravenous administration of 1 2 mgm provided a more rapid initial decline than after oral dose, but after three to four hours both effects were comparable Katz and Wise, Am Heart J, 30 125 (Aug.) 1945.

Myocardial Infarction All but one of 32 survived digitalization with 1 5-2.0 gm. digitalis in three to four days Askey and Neurath, J.A.M.A., 128: 1016; 1945.

DIGOXIN

Man—

Peripheral Arterial Embolism In two patients with mitral stenosis and auricular fibrillation 5 25 mgm and 0.5 gm digitalis over one week showed signs of overdosage in one Circulation of leg failed, gangrene and amputation. Second, 2 5 mgm digoxin in three days. Embolectomy accompanied arterial spasm Local sympathectomy recommended. Massey and Steiner, Lancet, 246 245, 1944.

DIHYDROTACHYSTEROL

Dogs—

Experimental Hypoparathyroidism 1 mgm/kg. produced an effect of greater magnitude and of about the same duration as 2 mgm/kg. of vitamin D₂ or D₃ McChesney and Giacomino, J Clin Investigation, 24: 680 (Sept.) 1945.

Man—

In Parathyroid Tetany: Minimal dose of 1 ml. daily raised blood calcium, prevented tetany and partially decreased laryngeal stridor. Harding, J. Lab. & Clin. Med., 27: 497 (Jan.) 1912.

Tetany Treatment: Dose determined by serum calcium level which should be kept at 9.5-11.0 mgm.%. If below 6 mgm.%, 30 drops (1 ml. = 30-35 drops) daily or 6 ml. weekly given, with serum calcium above 9 mgm.%, five drops daily or one ml. weekly. Tetanic symptoms with marked hypocalcemia, 8-15 ml. in a single dose, followed by a daily dose of 1 ml. Continuous parathyroid insufficiency cases required 10-30 drops daily or 2-6 ml. Holtz, J. Clin. Endocrinology, 1: 453 (May) 1911.

Tetany in Pregnancy: 0.5–1.5 ml. daily + 10 gm. daily of calcium lactate or gluconate. Parathyroid hormone with vitamin D may also be useful. Anderson and Musselman, *Am. J. Obst. & Gynec.*, 43: 547 (Apr.) 1942.

Bioassay: Determination of hypercalcemic effect on rats was found with error of 15–20%. McChesney and Kocher, *Endocrinology*, 30: 787 (May) 1942.

DIHYDROXYPHENYLALANINE

Rats—

Blood Pressure Raised: By intraperitoneal or intravenous injection of 12 mgm/kg. matched and sustained. Adrenalectomy abolished this response; bilateral nephrectomy enhanced magnitude and response. Page and Reed, *Am. J. Physiol.*, 143: 122; 1945.

3,5 DIODOSALICYLATE, SODIUM

In Vitro

M. tuberculosis: 1:25,000 concentration was four and a half times as active against *M. tuberculosis* as 1:7500 concentration of chaulmoogric acid. Kusand Wagner-Jauregg, *Biochem. Ztschr.*, 317: 256 (Sept.) 1944.

Rabbits—

Thyroid Effect: Subcutaneously, 25 gammas of iodine (in the form of drug) given for 16 days produced no increase in iodine levels of thyroids in two animals. *Ibid.*

DI-ISOPROPYL FLUOROPHOSPHATE

(D.F.P.)

Mice—

LD₅₀—Oral: 36.8 mgm/kg. \pm 0.98.

LD₅₀—Subcutaneous: 3.71 mgm/kg. \pm 0.16.

Horton et al., *J. Pharmacol. & Exper. Therap.*, 87: 414 (Aug.) 1946.

Rats—

LD₅₀—Intramuscular: 1.82 mgm/kg. \pm 0.09. *Ibid.*

Rabbits—

LD₅₀—Oral: 9.78 mgm/kg. \pm 0.65.

LD₅₀—Intravenous: 0.34 mgm/kg. \pm 0.01. *Ibid.*

Cats—

LD₅₀—Intravenous: 1.63 mgm/kg. \pm 0.03. *Ibid.*

General Effects: 1 to 8 mgm/kg., intravenously produced motor unrest, signs of apprehension, muscular twitching usually starting in head and neck region, head or body tremor, ataxia, weakness, pilomotor stimu-

lation, respiratory stimulation (panting) associated with labored respiration, salivation and defecation or diarrhea. These symptoms progressed with respiratory difficulty increasing and convulsions similar to those produced by camphor appearing prior to death resulting from respiratory and circulatory failure. Modell et al., *J Pharmacol. & Exper. Therap.*, 87: 400 (Aug.) 1946.

Eye: Miosis produced by 0.006 to 0.6 mgm. in one drop of aqueous solution which lasted ten days to two and one half months. *Ibid.*

Small Intestine in situ: One mgm/kg., i.v. lowest effective dose producing hyperactivity, which lasted for several hours. *Ibid.*

Dogs—

LD₅₀—Intravenous: 3.43 mgm/kg \pm 0.62

Horton et al., *J. Pharmacol. & Exper. Therap.*, 87: 114 (Aug.) 1946.

2–5 mgm/kg. intramuscularly in peanut oil produced skeletal muscle fasciculation but no evidence of muscarinic action. Koelle and Gilman, *J. Pharmacol. & Exper. Therap.*, 87: 421 (Aug.) 1946.

Monkeys—

0.2–0.3 mgm/kg. intramuscularly in peanut oil produced marked muscular fasciculation, rapid shallow respiration and diarrhea, but no miosis, excessive salivation, bradycardia, or apparent bronchial constrictions. *Ibid.*

DILANTIN SODIUM

(Sodium 5,5-diphenylhydantoinate (Phenytoin Na))

Mice—

Tolerance to Decompression Intraperitoneally, 1.0, 2.0, 3.0 mgm. prolonged the time tolerated to a pressure of 150 mm. Hg. Controls killed in an average of one minute and four seconds while with 2 mgm. dilantin, mice survived for an average of 15 minutes and 56 seconds. Hoff and Yahn, *Am. J. Physiol.*, 141: 7 (Mar.) 1911.

Rats—

Electric Epilepsy Hypodermic injection of 0.5 gm/kg raised threshold and prolonged clonic phases in rats subjected to electric shock and caused hyperglycemia. Delay and Soulaireac, *Compt rend Soc de biol.*, 138: 60 (Jan.) 1911.

Effect on Vitamin C By stomach tube 500 mgm/kg given to adult albino animals on vitamin C free diet, caused a peak of vitamin C excretion in urine on fourth day and decreased ascorbic acid content of tissues. Drake, Gruber, and Haurv., *J. Pharmacol. & Exper. Therap.*, 71: 268 (Mar.) 1911.

Rats (albino)—

Vitamin C Level: Orally, 500 mgm/kg. increased excretion of ascorbic acid in urine and decreased amount in tissues, especially adrenals, brain and skeletal muscle. Ibid.

Dogs—

Cardiovascular Depression: 0.005 gm. intravenously, caused arterial pressure to be lowered, slackened rhythm to momentary cessation of cardiac action up to 0.02 gm. Effects were temporary and reversible (sodium salt effect identical). Boudouin, J.A.M.A., 118: 1312; 1942.

Fatal: 66–69 mgm/kg. caused death. Scherf, Bull. New York Med. Coll., Flower & Fifth Ave. Hosps., 6:82 (June) 1943.

Man—

Epilepsy: 0.1 gm. two or three times daily according to age and increased 0.1 gm. a day at intervals determined by fit incidence. 24 of 43 showed complete cessation of fits in two months; 16 of 43 had drastic reduction of fits.

Toxic Manifestations: Skin reaction, mental changes; confusion, delusion, violence; neurological changes; nystagmus, ataxia, diplopia, myoclonus, slurred speech and tremors. Tullidge and Fox, Lancet, 243: 6 (July) 1942.

Kleptomania: 0.1 gm. dilantin sodium caused cessation of kleptomania and petit mal in a patient. Lawrence, Delaware State M. J., 14: 83 (May) 1942.

Bronchial Asthma: 0.03 gm. two times a day was increased to three times daily with persistence of symptoms. Dosage increased 0.03 gm. daily at one week intervals until symptom free. Usually 0.1–0.2 gm. daily was sufficient. Shulman, New England J. Med., 226: 260, 1942.

Epilepsy: Combination of 0.2–0.7 gm. and 0.05–0.35 gm. phenobarbital was given for three weeks to 31 months. Cases that did not respond to either drug alone were given in combination. Merritt and Brenner, J. Nervous & Mental Dis., 96: 245 (Sept.) 1942.

Fatal Case: Given 0.1 gm. three times daily for seven days, 0.2 gm. three times daily for three days died with a hemorrhagic erythema multiforma. Autopsy revealed extensive hemorrhagic changes in skin, mouth and gastroenteric tract and edema of lungs and brain. Ritchie and Kolb, Arch. Dermat. & Syph., 46: 856 (Dec.) 1942.

Poisoning: 0.10 gm. three times daily for 76 doses caused fever of 105° F., exfoliative dermatitis, marked enlargement of liver and spleen. Symptoms disappeared in one week. Handelbaum and Kane, Arch.

Neurol. & Psychiat., 45: 769; 1941, through J. Nerv. & Ment. Dis., 96: 215 (Aug.) 1942.

Gum Hyperplasia: Developed with 0.1 gm. three times a day for 13 to 16 months in two epileptic boys. Date, Proc. Roy. Soc. Med., 38: 567 (Aug.) 1945.

Pruritis Ani: Orally, capsules containing 0.1 gm. dilantin sodium, 0.33 gm. takadiastase, 0.02 gm. phenobarbital and 0.0025 gm. novatropine (homatropine methyl bromide) relieved 45 of 47 patients. Bodkin, Am. J. Digest. Dis. & Nutrition, 12: 255 (Aug.) 1945.

Pseudosclerosis: 0.032 gm. five times daily and phenobarbital 0.032 gm. three times daily maintained a case hospitalized after a Jacksonian convulsion. Peterman, Am. J. Dis. Child., 70: 114 (Aug.) 1945.

DILAUDID

(Dihydromorphinone hydrochloride)

Man—

Effect on Colon: Intramuscularly, 1–2 mgm. behaved same way as morphine. It increased tone and amplitude of the non propulsive type of rhythmic contractions and decreased propulsive activity of ileum and colon segments. Adler, Atkinson, and Ivy, Arch. Int. Med., 69: 974 (June) 1942.

2,3 DIMERCAPTOPROPANOL

(Radioactive B.A.L.)

Rats—

Excretion: Intramuscular injection of 20 mgm. radioactive B.A.L. in propylene glycol; the amounts of S^{35} present in urine at 6, 12, and 24 hours after injection were 45.5, 71.0, and 81.3% respectively. Smith, Science, 103: 439 (Apr. 12) 1946.

Percutaneous Absorption Rate of radioactive B.A.L. over a six hour period was 0.38 mgm/cm² skin per hour. Ibid.

DIMERCAPROL

(2,3 Dimercaptopropanol)

(B.A.L.)

Animals—

Best Therapeutic Procedure: Four injections B.A.L. at two to four hour intervals, followed by single daily injection for six days. B.A.L. in 1–10 mgm/kg. injection saved 55% of animals from repeated massive doses of mapharsen and delayed death in 22%.

Medical Application. Arsenical dermatitis or hemorrhagic-encepha-

litis following administration of mapharsen. Waters and Stock, Science, 102: 601 (Dec. 14) 1945.

Rats—

LD₅₀: 105 mgm/kg. intramuscular for American Reference Standard B.A.L. Ibid.

Protection: B.A.L. applied not later than two hours after applying two times LD₅₀ lewisite on skin (usually die in 24 hours) saved animal. Protection against systemic effect of lewisite by B.A.L. applied at skin site other than contaminated by lewisite or intramuscular B.A.L. in propylene glycol. B.A.L. applied to skin exerts antidotal action to sodium arsenite (2 times LD₅₀). Young, Science, 103: 439 (Apr. 12) 1946.

Man—

Arsenic Poisoning: Intramuscularly, B.A.L. in oil in 10% solution four injections at four hour intervals in 2.5–4.0 ml. doses. Reactions within 15–30 minutes after injection but do not contraindicate continuation of treatment. Bull. U. S. Army M. Dept. #88: 13 (May) 1945.

Tolerated intramuscular 10% or less in sterile peanut oil-benzyl benzoate solution. Inunction of 1 ml. of undiluted B.A.L. or 2 gm. in jelly base did not produce systemic effect. 3 mgm/kg. B.A.L. in oil, intramuscularly produce mildest reaction in few. Reactions, 5 mgm/kg. >50% nausea, vomiting, headaches, generalized aches and pains, burning sensation in mouth, nose and eyes, sweating, restlessness, weakness, pain in limbs, jaws and trunk muscles. Heart rate often increased, sometimes rise of blood pressure. Symptoms subsided in four hours. Waters and Stock, Science, 102: 601 (Dec. 14) 1945.

***β*-DIMETHYLAMINOETHYL-BENZILATE HYDROCHLORIDE**

Mice—

Toxicity: LD₅₀ was 39.9 ± 2.2 mgm/kg. intravenously, and 281.0 ± 15.1 mgm/kg. orally. Lee, Scott, and Chen, J. Lab. & Clin. Med., 30: 700 (Aug.) 1945.

Rats—

Toxicity. LD₅₀ was 29.2 ± 1.9 mgm/kg. intravenously, and $1,035 \pm 35.0$ mgm/kg. orally. Ibid.

Rabbits—

In Eyes: Intra-ocular administration of 0.05% solution dilated pupils and a 1.0% solution caused corneal anesthesia lasting from 15 to 20 minutes. Ibid.

Cats—

Dosage Levels: Intravenous doses of 1.0 mgm. had no effect on blood

pressure or respiration; 10 to 20 mgm. stimulated respiration and decreased blood pressure under light anesthesia, 5 to 10 mgm. increased blood pressure and depressed respiration, under deep anesthesia; 20 to 40 mgm. were usually fatal. Ibid

Intestinal Effects: Orally, 15 mgm/kg counteracted effects produced by 75 mgm/kg. of Syntropan. Ibid.

4-DIMETHYLAMINOSTILBENE

Rats—

Growth: 50 mgm/kg. retarded both body and tumor growth Haddow, Harris, and Kon, *Biochem. J.*, 39 11-111, 1945.

5,5-(1,3 DIMETHYLBUTYL)-ETHYL BARBITURIC ACID

Dogs—

Effect. 1-5 mgm/kg. augmented flexion and cross-extension reflexes in decapitated, decerebrated, and anesthetized animals. 2 mgm/kg. depressed the kneejerk in anesthetized animals and was stimulated by more than 5 mgm/kg. amounts. Knoefel, *J Pharmacol & Exper. Therap.*, 84: 26 (May) 1945.

DINITROPHENOL

(2,4-dinitrophenol)

Chickens—

Cataract: Produced in chick on diet containing 0.25% 2,4-dinitrophenol sodium; 1% 2,4-dinitro-6-aminophenol. or 0.5% 2,6 dinitrophenol caused fine grey opacity to be present in anterior part of lens on second and third day of feeding Robbins, *J Pharmacol. & Exper. Therap.*, 80: 364 (Mar) 1944.

DIDOQUIN

(5,7-duodo 8 quinolinol)

Man—

Amebiasis and Amebic Dysentery Successful treatment of 29 cases. D'Antoni, *Am. J. Trop. Med.*, 221 319 (July) 1912.

Amebic Dysentery and Trichomonas Infection Seven to ten tablets (0.21 gm) daily for 15 to 20 days Council of Pharmacy and Chemistry, *J.A.M.A.*, 123: 902, 1943

Toxicity: 0.8 gm., three times per day for 19 days in one patient developed furuncle 20 days after cessation of therapy, reappeared after treatment resumed. Furuncle developed in second patient, third patient received 2.4 gm. daily for 23 days and developed chills, fever, rash and blotchy erythema Silverman and Leshe, *J.A.M.A.*, 128 1080; 1945.

Amebic Hepatitis: 0.6 gm., three times per day for five days after treatment with 0.06 gm. emetine hydrochloride intramuscularly for six to ten times. Sodeman and Lewis, J.A.M.A., 129: 99; 1945.

DIODRAST

(1:1 mol. mixture of diethanolamine and 3,5-diiodo-4-(1)
keto-1-pyridineacetic acid)

Man—

Phlebography: 30 ml. of 35% solution. Anderson and Patterson, Northwest Med., 44: 178 (June) 1945.

Cerebral Angiography: 10 or 20 ml. Charest, J. de l'Hotel-Dieu de Montréal, 2: 101; 1944.

Excretion Urography: 20 ml. even in obese and muscular patients. Olin, Urol. & Cutan. Rev., 49: 220 (Apr.) 1945. Intravenously, 30 ml. Huff and Boger, J. Urol., 54: 116 (Aug.) 1945.

Cerebral Arteriography: Common carotid artery isolated under local anesthesia by a small incision just above and parallel to the clavicle; 10–12 ml. 35% Diodrast was injected and films taken during and immediately after. Incision closed with interrupted silk sutures; patient kept flat in bed for 24 hours. Gross, J. Indiana M. A., 37: 109 (Mar.) 1944.

Venogram: Injection of 15 to 20 ml. of 35% solution into a branch of the coronary vein was useful in confirming the site of origin of the coronary vein. Blakemore and Lord, Ann. Surg., 122: 476 (Oct.) 1945.

Cholangiographic Studies: Injection of 10 ml. into the common bile duct. Three plates were taken: one with the patient in the state of rest, one taken ten minutes after the injection of morphine and the third after the inhalation of amyl nitrite. The presence of stone, stricture, spasm and pancreatitis were shown. McGowan, Surgery, 18: 470 (Oct.) 1945.

DIPHENYLETHYLAMINES

Man—

Pain Relief: 200 mgm., orally every four hours relieved pain in seven, but five became mentally confused. 200–500 mgm. of β -hydroxy- $\alpha\beta$ -diphenylethylamine every four hours relieved pain in 12 cancer patients; induced sleep in eight. Dodds, Lawson, and Williams, Proc. Roy. Soc. Med. (London), 132: 119 (July) 1944.

DIPHENYLMETHANE

Monkeys (Rhesus)—

Laxative Activity: Of 23 compounds (indolines, anthraquinones, phthaleins). Ratio of action to monkey and man determined. Chemical

configuration and laxative activity. Locwe and Hubacher, Arch. internat. de pharmacodyn. et de thérap., 65: 297 (Mar.) 1911

DIPHTHERIA ANTITOXIN

Man—

Infectious Mononucleosis: 50,000 units plus 20,000 units penicillin every three hours obtained prompt reduction of temperature and clinical improvement. Levitan, Arch. Pediat., 62: 421 (Sept.) 1945

DIPHTHERIA TOXOID

Man—

Cutaneous Infection: (four cases resistant to usual therapy) Subcutaneously, 1 ml. aluminum precipitation toxoid to eczema with improvement. Second injection of 0.5 ml. caused striking improvement.

Mycosis Fungoides: Improvement with 1 ml. and subsequent 0.5 ml. injections.

Pemphigus: Improvement after three injections total 3 ml. Wise, Manhattan Dermatol. Soc. Meeting, Arch. Dermatol. & Syph., 45: 784 (Apr.) 1942.

Whooping Cough: Three injections of 0.5–1.5 ml. aluminum precipitated toxoid a week apart, dose depending on age (4–5 months–9 years old) reduced coughing attacks in 37 of 54. Turnbull and Varela, J. Pediat., 24: 46 (Jan.) 1944.

Prevention: Single dose 1 ml. aluminum precipitated toxoid gave immunity to 89% for at least 28 months following injection. 120 children injected 1.5 ml. followed by Schick test and 10% giving positive Schick test were given a repeat dose. Bull. Arch. Pediat., 59: 397 (June) 1942.

Immunization: 0.2 ml. initial dose, followed four to six weeks later by 0.5 ml. Great Britain, Ministry of Health, Circular (Apr. 1942), through Pharm. J., 148: 202 (June) 1942.

Intradermal Dose: 0.1 ml. Another dose in about three weeks advisable. Queries & Minor Notes, J. A. M. A., 119: 763, 1942

DIRAMIN

(An aqueous solution of the product resulting from the reaction between antimony catechol and triisopropanol amine in the presence of propylene glycol. 1 ml. = 8.17 mgm. Sb.)

Man—

Granuloma Inguinale: Intravenously, 2 ml. two to five times weekly effected slight healing to complete regression in 14 cases. Greenblatt et al., Ven. Dis. Inform., 26: 238 (Nov.) 1945.

DITHIOBIURET**Rats—**

Lethal Doses: Single subcutaneous or intraperitoneal injections of 20 to 50 mgm. Repeated administration of less than 0.5 mgm. subcutaneously or in drinking water caused fatal paralysis. Astwood et al., Science, 102: 196 (Aug. 24) 1945.

DORYL

(Choline chloride carbamate)

Man—

Skin Sensitivity: In young women more than in men when ionized into skin. Lewis, Clin. Sc., 5: 5; 1944.

Glaucoma: 1.5% in 0.03% alkyl dimethyl-benzyl ammonium chloride (zephiran) twice daily either alone or with pilocarpine reduced intraocular pressure to normal after pilocarpine and/or eserine failed. Hardesty, Am. J. Ophth., 27: 625 (June) 1944.

Peripheral Vascular Disease: Subcutaneously, 0.25 mgm. twice weekly for six months to three years to 21 patients definitely relieved rest pain. *Contraindicated* in asthma, chronic bronchitis and peptic ulcers. *Sensitivity* tested with 0.125 mgm., then 0.25 mgm. Saland et al., Ann. Int. Med., 23: 48 (July) 1945.

DYSENTERY TOXOID (SHIGA)**Man—**

Reactions: 142 volunteers had headache, chills, muscular soreness, urinary frequency, nausea, vomiting and pyrexia.

Administration: Most effective is 0.25 or 0.5 ml. in three spaced doses at three week intervals with recall dose in three months (93% had detectable antitoxin ten days later in subject with injections at three week intervals). Farrell, Fraser, and Ferguson Canad. Pub. Health J., 35: 311 (Aug.) 1944.

SHIGELLA PARADYSENTERIAE FLEXNER ENDOTOXIN**Mice—**

Susceptibility and Age-Weight: 12, 20, 35 gm. mice; 25, 50, 350 days were killed by the same minimal amounts of endotoxin. Death was due to disabling of a single physiologic system independent of age or body weight. Zahl, Hutner, and Cooper, Proc. Soc. Exper. Biol. & Med., 54: 137 (Oct.) 1943.

ACETYLATED SHIGELLA DYSENTERY ANTIGEN (SHIGA)**Mice—**

Toxicity: Undetoxified Shiga soluble antigen 0.4 mgm., four of four died; 0.2 mgm., three of four died, 0.1 mgm., no deaths, but weight loss of 13% by third day; 0.05 mgm., a 6% weight loss for three days. *Acetylated Derivatives:* 3 mgm. did not kill any of 48 mice. Weight losses varied from 0–10%, therefore toxicity was 60 times less than original. Treffers, Science, 103, 387 (Mar 29) 1916.

Immunization: Subcutaneous or intraperitoneal of three 0.05 mgm. acetylated fractions protected 19 of 93 or 20% given 1.5–4 hours and 61 of 151 or 42% given five to 24 hours after intracerebral administration of live Shiga organisms (four of 55 controls and four of 15 given toxic Shiga antigen). Ibid.

Rabbits—

Toxicity: Undetoxified Shiga antigen—single injection of 0.005 mgm. produced 2.7° C. temperature rise with characteristic initial leucopenia followed by leucocytosis, and repeated injections caused 3.6° C. temperature rise and leucocytosis of 36,000 after 18 hours. Acetylated antigen—0.3 mgm. less highly acetylated antigens produced responses equal to 0.005 mgm. of toxic material, while insoluble fractions caused 1.6° C. temperature rise and leucocyte counts of 12,000. Ibid.

EMETINE**Man—**

Amebiasis: Subcutaneously or intramuscularly not more than 0.06 gm. daily during diarrheal phase for no more than four to six days. Carbarsone was given concurrently in doses of 0.25 gm. three times daily for seven days, except in patient with hepatic disease. Diodoquin or chiniofon may be substituted for carbarsone in 0.63 and 1 gm. respectively three times per day for seven days. U. S. War Dept. Tech. Med. Bull., 159; War Med., 7: 390 (June) 1945.

90% of 523 patients were successfully treated subcutaneously with 0.065 gm. two times a day for three days, and the same amount for two days after one week interval. Risk of toxic reaction was 0.05%, if not >0.65 gm. was exceeded in one month. Simultaneously, 0.25 gm. carbarsone orally, two times a day for ten days, repeated two times within a ten day interval. If failed to improve, chiniofon was given, 1 gm. three times daily for one week in three courses at seven day intervals or diodoquin, 0.6 gm. per day for ten days, repeated after one week. Brown, North Carolina M. J., 5: 1 (Jan.) 1911.

Treatment consisted of subcutaneous 0.06 gm. emetine hydrochloride given daily for ten days and daily with either 0.5 gm. chiniofon twice daily orally for ten days or 0.25 gm. carbarsone three times daily for seven days. With the last two, retention enemas of 2% chiniofon and of 1% carbarsone plus 2% sodium bicarbonate respectively were given. Turner, Kentucky M. J., 42: 135 (May) 1944. (See Payne, Lancet, 248: 206 (Feb.) 1945.)

Acute Amebic Dysentery: Intramuscularly, emetine hydrochloride, 0.065 gm. per day for ten days. Carbarsone, 0.025 gm. three times daily was started on fifth day and continued for seven days. A second course required after seven day rest. Ivy et al., U. S. A. Military Surgeons Meet. Clinics, 2: 1219 (Feb.) 1944.

Amebic Hepatitis: Intramuscularly, emetine hydrochloride, 0.06 gm. six to ten times daily followed by diodoquin, 0.6 gm. three times daily for five days. Sodeman and Lewis, J.A.M.A., 129: 99; 1945.

Lung Irritants: Subcutaneously, 4 mgm. emetine hydrochloride plus liberal oxygen inhalation against phosgene. McConnell, New York State J. Med., 42: 350; 1942.

"T" Wave Depression: All leads; noted in 52.7% of 72 patients on 0.03 gm. emetine hydrochloride subcutaneously twice daily for ten days (amebic dysentery). Hardgrove and Smith, Am. Heart J., 28: 752 (Dec.) 1944.

Therapy of Amebic Liver Abscess: Intravenously or intramuscularly, 0.06 gm. for six days, then a rest for six days, the course repeated as necessary. Berne, Surg., Gynec. & Obstet., 75: 235 (Aug.) 1942.

EMETINE IODOBISMUTHATE

Man—

Amebiasis. Orally, 0.13–0.18 gm. each night for ten times; patient fasted for four hours previously. Sedative was given one-half hour before. A retention enema containing 2.5% chiniofon in 200 ml. warm water after breakfast and lower bowel cleaned with 2% sodium bicarbonate enema. Manson and Bahr, Lancet, 247: 718 (Dec.) 1944.

Chronic Amebic Dysentery: 47 cleared after intramuscular injection of 100,000 units penicillin initially, followed by 33,000 units every three hours (total 2,000,000 units) and sulfasuxidine orally, total of 80 gm. 12 day course of emetine bismuth iodide together with daily retention chiniofon enmata followed by acetarsone or carbarsone, 0.25 gm. twice daily for 12 days Hargreaves, Lancet, 249: 68 (July) 1945.

ENCEPHALITIS ANTISTREPTOCOCCIC SERUM**Guinea Pigs—**

Equine Encephalomyelitis 67.3% recovery with 500–1000 units specific hyperimmune rabbit serum. 40 of 41 controls died. Zichis and Shaughnessy, *Am. J. Pub. Health*, 35 815 (Aug) 1945.

Monkeys (Rhesus)—

Equine Encephalomyelitis 45.5% recovery rate and 0% for controls with hyperimmune rabbit serum *Ibid.*

Man—

Epidemic or Postoperative Hiccup 90 cases given concentrated serum with good results. Rosenow, *J. Lab. & Clin. Med.*, 28 277 (Dec.) 1942.

ENTEROCRININ

(Hormone factor which controls secretion of succus entericus)

Dogs—

Threshold Dose 50–80 micrograms stimulated intestine but not the pancreas. Nasset, *Rev. Gastroenterol.*, 9 188, 1942

EPHEDRINE**Cats et al.—**

Cardiovascular Response Perfused frog heart, perfused rabbit ear, blood pressure of cat, limb volume of cat. Small concentrations increased action of corresponding autonomic substance and in higher concentrations diminished these actions. At 0.05 mgm–0.5 mgm/kg. effect of ephedrine changed from increase to decrease in epinephrine activity. Graham and Gurd, *J. Pharmacol. & Exper. Therap.*, 72: 48 (May) 1941.

Man—

Hypersensitivity. Eruption around nares spread to other parts of face and body when 1% oily nose drops were used. Spencer, *Arch. Dermat. & Syph.*, 31: 48 (Jan.) 1945.

Red Blood Cell Count. Orally, 50 mgm of sulfate per day for three to four weeks, to seven normal, physically active men caused mild polycythemia. White blood cells were not uniformly changed. In those given drug longer than four weeks, the red blood cell count receded toward normal. Harris and Davis, *Proc. Soc. Exper. Biol. & Med.*, 51: 195 (Nov.) 1943.

Use with Epinephrine (in spinal anesthesia) Intramuscularly, 25–50 mgm. was ineffective, but 0.2 mgm epinephrine given intramuscularly with ephedrine, or up to 55 minutes after ephedrine, gave desired blood pressure rise. Rochberg and Apgar, *Anesthesiology*, 3 49 (Jan.) 1942.

EPINEPHRINE

Frogs—

Assay: Isolated, perfused hearts from the winter male animals were used. The same tissue was used for test and standard solutions, each perfusion lasted for one and a half to two minutes. The standard gave an adequate response in a concentration of 1/100 million epinephrine. West, J. Physiol., 102: 367 (Dec.) 1943.

Mice—

Hypnosis: Prolonged with 0.04 mgm/kg. epinephrine or 0.05 unit insulin intraperitoneally or intramuscularly 20 minutes prior to intraperitoneal injection of 100 mgm/kg. evipal soluble. Slept 1.5 times as long as mice receiving evipal alone. Reinhard, Proc. Soc. Exper. Biol. & Med., 58: 210 (Mar.) 1945.

Rats—

Diuresis: Injection of 30–150 microgram/100 gm. body weight greatly increased the polyuria induced by hourly injection of standard water dose in normal animals. With water given at half-hour intervals, diuresis was less pronounced and water intoxication occurred. In adrenalectomized animals given water, increased diuresis was less marked and water intoxication was prevented. Gaunt, Liling, and Cordsen, Endocrinology, 37: 136 (Aug.) 1945.

Toxicity: Epinephrine hydrochloride solution, 1:1,000, LD₅₀ by subcutaneous route was 5 mgm/kg.; intramuscularly, 3.5 mgm/kg. Richards, Fed. Proc., 1: 71; 1942.

Rabbits—

Ulcer Production: Intramuscularly, 2 mgm. powder daily or intravenously, 1.5 ml. human breast or omental fat/kg., or administration of pitressin and obstruction of the portal circulation sensitized animals to ulcers. Wangenstein, Canad. M. A. J., 53: 309 (Oct.) 1945.

Cats—

Loss During Anesthesia. Rate of epinephrine loss was 2.7% per hour after 1.5 mgm morphine hydrochloride, and intravenously, 5% pentobarbital, 6.7% per hour with ether, and 4.45% per hour with cyclopropane. Elmes and Jefferson, J. Physiol., 101: 355 (Nov.) 1942.

Experimental Shock obtained by manipulation of small intestines, was reduced, and survival rate increased 300% by 2 mgm/kg. intramuscular, two to three hours preceding manipulation. Kabat and Freedman, Proc. Soc. Exper. Biol. & Med., 46: 385 (Mar.) 1941.

Cats and Dogs—

Bioassay. Intravenously at juncture of saphenous and femoral veins,

0.3 to 1.0 ml. for cats and 0.5 to 1.5 ml. for dogs of diluted standard and test solutions, injected alternately every five minutes and kymograph record was made. Dose of standard was amount which produced submaximal response equivalent to blood pressure rise of 50 to 70 mm. of mercury. Responses on kymograph were measured to nearest millimeter and computed mathematically. Thompson, *J. Am. Pharm. A.*, 34: 265 (Oct.) 1945.

Dogs—

Continuous intravenous injection of 1:5000 solution at rate of 0.01 mgm./kg. per minute for one hour produced shock. Scholz et al., *J. Clin. Investigation*, 24: 154 (Mar.) 1945.

Bioassay: Standard Reference Solution of 1:50,000 or 1:100,000 dilutions and similar dilutions of the unknown were injected at five-minute intervals into the saphenous vein. A simple chart and nomograph were used for making the necessary calculations. Knudsen et al., *J. Pharmacol. & Exper. Therap.*, 86: 339 (Apr.) 1946.

Bioassay using progressively increasing doses. Log dose-response curves given. Hjort, De Beer, and Randall, *J. Pharmacol. & Exper. Therap.*, 71: 105 (Feb.) 1941.

Bioassay: Varying doses of the solution injected into the anesthetized animal to produce consistent rises in blood pressure of 30–80 mm. Hg to determine the dose which caused a rise of 30–45 mm. Hg (S_1). From the rise caused by a dose twice S_1 (S_2) and two doses of the unknown solution (U_1 and U_2) such that $S_1 \cdot (S_2) \approx U_1 \cdot U_2$, the potency of the unknown solution was determined with an average deviation from the true value of 1.43%. Noel, *J. Pharmacol. & Exper. Therap.*, 84: 278 (July) 1945.

Man—

Anxiety States. Intravenous test dose of 0.01 mgm. followed by 0.5 ml. 1:1000 solution usually twice daily, then reduced to once daily, then three times a week, once weekly, finally once every two to four weeks, and dosage increased to an average single dose of 1–1.5 ml. benefited nine of 19 cases. Cameron, *Am. J. M. Sc.*, 210: 281 (Sept.) 1915.

Parkinsonism. Intravenously, 0.1 or 0.2 mgm. daily for ten days, repeated after three to five days.

Rheumatic Chorea in Children. Intravenous small doses eight days and in a few cases 0.1 mgm. daily for the 1st month. Serrano, *Polichinico*, 48: 289 (Feb.) 1942. *Anal.*, 21: 199; 1942.

Asthma: 0.5 ml. of 1:1000 solution every 15 mi

radiated injection
occurs thro-

doses and then discontinued if relief was not obtained in one hour. (See helium and dextrose.) Peters, Illinois M. J., 82: 428 (Dec.) 1942.

Infant Dose (under one year): Hypodermically, 0.10 ml. of 1:1000 epinephrine hydrochloride. If relief was not obtained, 0.15 gm. was given in 15–20 minutes then increased by 0.05 ml. every 15 or 20 minutes until relief was obtained. At this age not more than 0.20–0.30 ml. should be given. Questions & Answers, Ann. Allergy, 1: 170 (Sept.-Oct.) 1943.

Hunger: and acute dyspepsia, produced in healthy subject given orally, 3 mgm. in 6 ml. of 35% alcohol. Ibid.

Hyperinsulinism: Subcutaneously, 1 mgm. increased blood sugar levels. 1 mgm. two times a day prevented hypoglycemic convulsions Conn and Conn, Arch. Int. Med., 68: 1105 (Dec.) 1941.

"T" Wave. Subcutaneously, 1 ml. 1:1,000 solution to five normals lowered all "T" waves with maximal effect in 10–15 minutes. Hartwell et al., J. Clin. Investigation, 21: 409 (July) 1942.

Hypersensitivity: (Nervous and mental symptoms with muscular incoördination). Few minutes after subcutaneous administration of 0.5 ml. of 1:1,000 hydrochloride; duration, two hours to five weeks (facial palsy) Oral ephedrine sulfate before injection may have predisposed. Appelbaum, J. Allergy, 15: 392 (Nov.) 1944.

Asthma. 0.3 ml. dose of 1:1,000 dilution was repeated as often as necessary without untoward reactions. Walton, Manitoba M. A. Rev., 25: 370 (Sept.) 1945.

0.2–1.0 ml/oil—response in ten to fifteen minutes Bacon, Stickler, and Lamson, J. Allergy, 13: 48 (Nov.) 1911.

Gastric Pam: Produced in six patients with achylia by oral administration of 2 mgm. in 4 ml. 35% alcohol. Brun, Acta med. Scandinav., 113: 163, 1943.

ERGONOVINE

Assays—

Colorimetric using p-dimethylaminobenzaldehyde. Powell et al., J. Am. Pharm. A., Sci. Ed., 30: 255 (Oct.) 1941.

Biologic, isolated rabbit uterus. Ibid.

panc. tion from other alkaloids and ether-water distribution. Grove, J. Am. Pharm. A., 30: 260 (Oct.) 1941.

was reduced, an

muscular, two to three

man, Proc. Soc. Exper. Bi mgm. every four hours for six doses immediately
Cats and Dogs— ment in bed encouraged. Rotstein, J. A. M. A., 125

Bioassay: Intravenously

Labor: 0.2 mgm. intravenously, after fetal head

delivered (1020 cases) 81% lost no more than 100 ml. blood and third stage lasted for three minutes or less in 73% Davis and Boynton, *Am. J. Obst. & Gynec.*, 43: 775 (May) 1942.

Effect on Pregnancy 0.1 mgm. or two units ergotrate (ergonovine hydracrylate) caused in eight of ten pregnant women a moderate amount of interference with relaxation and in two, severe uterine tetany Woodbury et al., *J. Pharmacol. & Exper. Therap.*, 80: 256 (Mar) 1914

IRRADIATED ERGOSTEROL

Rats—

Chronic toxicity of electrically-activated vaporized ergosterol at 20,000 international units per kg. daily for 127 times produced no histologic change nor did 20,000 international units per kg. daily for 190 days show discernible radiologic alterations in body structures. No signs of toxicity. Reynolds and Burns, *Indust. Med.*, 12: 835 (Dec.) 1913.

Man—

Poisoning: 750,000 units (containing 50% calciferol, 50% mixture of lumisterol, tachysterol and toxisterol) daily in milk. In 12-17 days, nausea, vomiting, and abdominal pain. Urine contained hyaline casts and red blood cells. Blood serum calcium = 15 and 18 mgm/100 ml. P = normal. Therapy forcing of fluids, low calcium diet. Tumulty and Howard, *J.A.M.A.*, 119: 233; 1942.

ERGOTAMINE TARTRATE

(Gynergen)

Man—

"T" Wave: Subcutaneously, 1 ml. in two normals caused marked nausea. When 0.5 ml. was given "T" waves of all three leads of five subjects were raised without marked slowing of pulse. Maximal effect in 30-60 minutes Hartwell et al., *J. Clin. Investigation*, 21: 409 (July) 1942.

Migraine. 0.25-0.5 mgm intravenously to 16 patients gave subjects relief in eight to 15 minutes. Forced fluids, 15 liters water in five to ten minutes brought diuresis and relief of headache. Redisch and Pelzer, *Am. Heart J.*, 26: 598 (Nov) 1913. Hypodermically or intramuscularly, 0.25-0.50 mgm. in 1:2,000 solution relieved pain in 40-90 minutes in 60-80% of patients. Palmer, *Clinics*, 4: 531 (Aug) 1915

ERYTHROGENIC TOXIN

Children—

Active Immunization Against Scarlet Fever Three graduated injections of purified tannic acid precipitated hemolytic streptococcus erythro

genic toxin 750; 3,000; 10,000 units at two week intervals and in 0.1 ml. doses intradermally.

Adults—

500; 3,000; 6,000; 10,000 units of same volume and same interval. Veldie, Peck, and Franklin, Pub. Health Rep., 56: 957 (May 2) 1941.

ERYTHROIDINE HYDROCHLORIDE

Man—

Catatonic Pupil: Intravenously, at rate of 400 mgm. per minute caused pupillary changes. 1.5 gm. was sufficient to modify metrazol shock. Levine and Schilder, J. Nerv. & Ment. Dis., 96: 1 (July) 1912.

ESIDRONE

(Mercurial Diuretic)

Cats—

Fatal: 0.21 ml/kg. intravenously; without theophylline 0.27 ml/kg. intravenously (1 ml. = 40 mgm. Hg.). De Graff and Lehman, J.A.M.A., 119: 998; 1912.

α -ESTRADIOL

Rabbits—

Uterine Endometrium: Total dosage of 180–297 micrograms rendered uterine mucosa of inseminated ovariectomized animals sensitive to progesterone and did not interfere with the response when given simultaneously. Werthessen and Gargill, Endocrinology, 37: 15 (July) 1915.

Man—

Suppression of Lactation: Sublingually, 2.5 mgm. four times per day (10 mgm. daily) in propylene glycol. 61 puerperal cases. Diddle et al., J. Clin. Endocrinology, 2: 307 (May) 1942.

Drops, Sublingually: Endothelial proliferation with dose of 150–195 mgm. for castrates, 120–150 mgm. for patients with secondary anemia, given during 20 days. Menopausal symptoms abolished with 50 mgm. and lactation inhibited with 12 mgm. Reifferscheid and Schmidt, Klin. Wchnschr., 20: 440 (May) 1911.

Qualitative Determination of Estradiol Benzoate: Schorl's method—Evaporate a sample with fuming nitric acid, reduce with aluminum and stannous chloride and treat with sodium nitrate. The addition of 1, 8-dihydroxy-naphthalene-3, 6-disulfonic acid produced an intense red violet color. 2 mgm. gave a definite test; the reaction was specific. Malowan, J. Am. Pharm. A., (Scient. Ed.) 34: 245 (Sept.) 1945.

ESTRADIOL BENZOATE

Rana Pipiens (newly metamorphosed)—

Effect: Injection 0.03 mgm. dissolved in sesame oil at weekly intervals for four weeks inhibited growth of ovaries and stimulated gonads of both sexes. Implantation of whole pituitaries from adults caused immature testes to grow five to ten times and ovaries two to three times that of controls. Shreiber and Rugh, *J. Exper. Zool.*, 99: 93 (July) 1945

Mice—

Continued Administration: Injection of 100–200 rat units for 2.5–7.75 months produced tumors and precancerous tissue changes in 200 rat units and less marked tissue changes in 100 rat units. Crossen and Loeb, *Arch. Path.*, 37: 202 (Mar.) 1944.

Man (Women)—

Menopause: Intramuscularly, 10,000 international units every other day for the first week or until flushes have ceased then every third day and later reduced to 5,000 units. Drips, *Lancet*, 62: 437 (Dec.) 1912.

Bullous Lichen Planus. Treated with 2,000 rat units crystalline estradiol benzoate in sesame oil per week for five weeks. Zugerman and Gross, *Pennsylvania M. J.*, 47: 571 (Mar.) 1914

ESTRADIOL DIPROPIONATE

(Diovo cyclin)

Rats—

Experimental Hepatic Cirrhosis. Administration of four doses of four micrograms produced striking changes in testes of these animals, although similar doses to normal animals caused no damage. Morrione, *Arch. Path.*, 37: 39 (Jan.) 1944.

Mammary Structure. Five micrograms daily for ten days caused dilation of the lateral buds or increased their numbers in normal and castrated male rats after adrenalectomy. Reeder and Leonard, *Proc. Soc. Exper. Biol. & Med.*, 55: 61 (Jan.) 1914

Man—

Dysmenorrhea. Temporary relief with 10 mgm. injected at sixth day of cycle, repeated in groups of three injections at ten day intervals. Continued three months only. Sturgis and Meigs, *Surg., Gynec. & Obst.*, 75: 87 (July) 1942

Angina Pectoris. Five mgm. at four and five day intervals for 12 injections brought improvement. Strong and Wallace, *Canad. M. A. J.*, 50: 30 (Jan.) 1944.

ESTRIN

(3-hydroxy-17-keto- Δ 1,3,5-estradiene)

Man—

Purpura: Intramuscularly, 10,000 international units estrin twice weekly for three weeks and once weekly in one patient thereafter for two months caused cessation of purpura manifestation. Farrar and Roxby, *Clinics*, 2: 1295 (Feb.) 1944.

ESTROGENS

Guinea Pigs—

Assay—Unsuitable: Guinea pig unit 0.5 mgm. equals 150 times rat unit (0.0033 mgm.) and 5500 times mouse unit (0.00009 mgm.). Unit equaled dose which produced full vaginal cornification in 50% of animals when hormone was given subcutaneously in sesame oil in four fractions over 36 hours. Bell and Knox, *J. Endocrinol.*, 2: 399 (Sept.) 1941.

Antifibromatogenic Activity: 15 microgram, progesterone; 90 microgram, desoxycorticosterone; 100 microgram, dehydrocorticosterone; approximately 200 microgram, testosterone or approximately 100 microgram, dihydrotestosterone absorbed daily prevented growth of abdominal fibroids in 80% of guinea pigs receiving estrogens. Lipschütz, *Nature*, 153: 260 (Feb.) 1944.

Man—

Implantation Therapy: 59.4 mgm. per patient for treatment of menopausal syndrome; 93.4% of 45 patients satisfactory; 53.5 gm. per patient with improvement in all of 12. Bennett and Te Linde, *J.A.M.A.*, 118: 1341; 1942.

Breast Engorgement: Orally, 3.75 mgm. every four hours for five doses of natural estrogen (Premarin) prevented engorgement in 30 patients and proved just as effective as diethylstilbestrol. Meek and Murby, *Canad. M. A. J.*, 50: 241 (Mar.) 1944.

Rectal Strictures: Orally, 30 mgm. p-hydroxyphenyl ethyl hexane daily for five weeks and 18 mgm. hydroxyphenylhexane daily for two months gave response in one patient. Large doses to three others. Seley, Vernick, and Goldman, *J. Clin. Endocrinol.*, 5: 301 (Sept.) 1945.

Mice—

Assay: By uterine weight response. Evans, Varney, and Koch, *Endocrinology*, 28: 747 (May) 1941.

Bile Duct Enlargement with estradiol dipropionate and benzoate in oil. (16.6–50 microgram weekly) estrone pellets or stilbestrol (250 micro-

gram weekly). Gardner, Allen, and Smith, *Proc. Soc. Exper. Biol. & Med.*, 46: 511 (Mar.) 1941.

Chickens (Single Comb White Leghorn)—

Genital Tract: 0.25 mgm. intramuscularly caused growth. Herrick, *Poultry Sci.*, 23: 65 (Jan.) 1944.

Spayed-rat Assay Method: Priming with one microgram weekly of estrone in 0.1 ml. sesame oil followed by 0.25 ml. sesame oil solution of standards and unknowns containing up to one microgram theelin or equivalent. Reliable vaginal smears may be obtained 48–52 hours after injection of standards and unknowns. Koch and Otway, *Endocrinology*, 31: 162 (Aug.) 1942.

Rats—

Absorption: Subcutaneously, intramuscularly, intraperitoneally, 5.0 mgm. estradiol in 0.1 ml. paraffin into 76 females (three to five weeks), were absorbed in 151 ± 5.9 days as demonstrated by vaginal smears. Eisen, *Proc. Soc. Exper. Biol. & Med.*, 19: 625 (Apr.) 1942.

Ovary Weight was increased with subcutaneous injection of stilbestrol (1), 9 mgm.; or α estradiol dipropionate (2), 1.5 mgm. three times daily but not with 6,000 international units estrone. When (1) and (2) were given in high doses prior to administration of chorionic hormone, there was a significant increase in ovarian weight Fluhmann, *Proc. Soc. Exper. Biol. & Med.*, 47: 378 (June) 1941.

Tumoral Reaction: Subcutaneously, 80 microgram estradiol monobenzoate was given three times weekly for three months to "young" castrate females (180–215 gm.). In "aged" (700–1,050 gm.) animals, the incidence of uterine and extragenital fibroids were no less when the same amount of estradiol monobenzoate was given. Lipschutz and Vargas, *Proc. Soc. Exper. Biol. & Med.*, 48: 581 (Dec.) 1941

Man—

Use in Threatened Abortion: 30,000–100,000 rat units of estradiol benzoate and 100–200 mgm. stilbestrol were injected into the anterior lip of cervix, plus oral administration of 0.5 mgm. estradiol, every 15–30 minutes until uterine contractions relieved. 14 of 25 went to full term. Karnaky, *Texas State J. Med.*, 37: 113 (Oct.) 1941

Appraisal: Oral and parenteral—*Oral*, capsule containing 0.5 mgm. crystalline estrone in oil (5000 international units) *Parenteral* 5.0 mgm. crystalline estrone in aqueous suspension, each ampule equals 50,000 international units. Maximum response was obtained more rapidly after oral administration (54 days) than after injection (eight days) but maxi

num effect remained 14 days after injection and only two days after oral administration. Orally in divided doses, maximum reaction was produced as rapidly as injected and sustained longer than single doses. No toxic effect after oral use. Mack and Ale, *J. Clin. Endocrinol*, 2: 361 (June) 1942.

Carcinoma of Prostate: Orally, 1 mgm. stilbestrol three times daily for two to three weeks followed by 2 mgm. daily for two to four weeks and 1 mgm. daily thereafter brought clinical improvement, gain in weight, improvement in blood picture, decreased pain, and decreased size of gland. Orally, 0.05 mgm. three times daily, ethinyl estradiol for several weeks, reduced to 0.05 mgm. (two times daily) for several weeks, and then 0.05 mgm. indefinitely, produced similar results. Kearns, *Wisconsin M. J.*, 41: 575 (July) 1942.

Estrogen Response: Gauged by staining. Vaginal smear stained by laying slide face down over shallow pan containing Lugol's solution two to three minutes. Mack, *Harper Hosp. Bull* (Detroit, Mich.), 1: 54 (Jan.) 1942.

Gonorrheal Vulvovaginitis: 0.2-1 mgm. one to three times a week to children, 15,000 international units before cornification became apparent. All children bacteriologically and clinically controlled. Brown, *Am. J. Dis. Child.*, 64: 221 (Aug.) 1942.

Hyperthyroidism: 50,000 international units two times weekly for six weeks to three months produced favorable response. Estrogen plus iodine relieved symptoms of exophthalmic goitre and produced remission. Rocca and Falcone, *Rev. Asoc. méd. argent.*, 55: 434 (June 15) 1941; through *J.A.M.A.*, 117: 1742 (Nov. 15) 1941.

Hyperthyroid Adjuvant. Intramuscularly, 10,000 estrogenic units of estrone (theelin) in oil daily for two to three days before operation. Post-operative course better than controls. Stork and Holcombe, *Surgery*, 11: 703 (May) 1942. Stork and Sabatier, *Ann. Surg.*, 115: 821 (May) 1942.

Menstrual and Reproductive Disorders: Improvement with 100 international units initial dose continued daily and not in excess of 300 international units produced improvement. Schneider, *J. Clin. Endocrinol.*, 2: 120 (Feb.) 1942.

Pituitary Disease: 10,000 rat units injected at not more than three-day intervals. Goldzieber, *Pennsylvania M. J.*, 45: 687 (Apr.) 1942.

Senile Pruritis Therapy (with estrogens and androgens): Subcutaneously, 10 mgm. testosterone propionate was given plus 1 ml. estradiol benzoate or estradiol dipropionate, subcutaneously. Feldman, Pollock, and Abarbanel, *Arch. Dermat. & Syph.*, 46: 112 (July) 1942.

Tinea Capitis Treatment. Orally, 5,000 international units daily for 14-56 days and stilbestrol, 3 mgm. daily for 7-63 days. 125,000 international units of stilbestrol per 31 gm. as ointment, total dose of 30 to 210 gm. Poth and Kaliski, Arch. Dermat & Syph., 45: 121 (Jan.) 1942.

ESTRONE

(Theelin)

Man—

Hyperthyroidism. 1,550,000 international units was given in two and a half months to a patient with a mild exophthalmic goitre and another was given 800,000 international units in three months. Both had complete remissions with no relapses 17 and 25 months, respectively, after treatment. No response was obtained in severe thyrotoxicosis cases. Farbman, J. Clin Endocrinol, 4: 17 (Jan) 1944.

ETHINYL ESTRADIOL

Man—

Climacteric: 0.05 mgm enteric coated ethinyl estradiol daily for 21 days controlled symptoms during 348 cycles in 45 women. Lyon, Am J. Obst. & Gynec., 47: 532 (Apr) 1944.

ETHINYL TESTOSTERONE

Man—

Effect on Cervical Secretion. 10 mgm of 17-ethinyl testosterone twice daily for six to ten weeks changed cervical mucus pH from 5 to 6 to pH 7 to 8 in five of six patients Birnbeig, Kurzsok, and Weber, Am. J. Surg., 57: 180 (July) 1942

ETHYL AMINO-BENZOATE

Man—

Thrombidiosis (chigger bites) Two parts in 15 parts flexible collodion relieved itching for four to eight hours. Sutton, J A.M.A., 120: 26; 1942.

ETHYLAMINOLEATE

(Etalate)

Man—

Varicose Vein Therapy 5% solution used in 150 patients with results equal to or better than those obtained with other solutions. Bowman, Ontario M. Rev., 10: 217 (Dec.) 1943.

ETHYL BROMIDE

Rats—

Toxicity: Oral doses up to 1200 mgm/kg. were not toxic. Miller and Haggard, J. Indust. Hyg. & Toxicol., 25: 423 (Dec.) 1913.

ETHYL ETHER

Rats—

Effect of Hemorrhage: Loss of more than 25% blood volume reduced the induction time to 60, 65 and 75% of the normal time in ether concentrations of 7, 8 and 9%. Anesthesia could be maintained in 50% bled rats with 3-4% ether concentration while 5-6% concentration was required for 50% anesthesia of normal. Wood and Jaco, J. Pharmacol. & Exper. Therap., 79: 259 (Nov.) 1943.

Blood Counts: Unaltered significantly by one to two minutes or 60 minute period of light or deep anesthesia. Crafts, J. Lab. & Clin. Med., 29: 1070 (Oct.) 1944.

Rabbits, Cats, Dogs—

Respiratory Tract Fluid: Subcutaneously, atropine sulfate 50-500 mgm/kg. for rabbits, 1-20 mgm/kg. for cats and 1-4 mgm/kg. for dogs markedly reduced saliva flow which was greatly increased with ether, but had little or no effect on fluid flow. Boyd and Munro, J. Pharmacol. & Exper. Therap., 79: 346 (Dec.) 1913.

Dogs—

Plasma Volume and interstitial fluid decreased even after morphine and atropine premedication. Bonnycastle, J. Pharmacol. & Exper. Therap., 75: 18 (May) 1942.

Man—

Blood Concentration at Term: 0.680 gm./liter in blood from umbilical vein, 0.713 gm./liter in venous blood of mothers; 0.374 gm./liter in umbilical artery of 33 infants. Smith and Barker, Am. J. Obst. & Gynec., 43: 763 (May) 1942.

Blood Levels in Surgical Anesthesia: At second plane, third stage 50-130 mgm.%, average 80-100 mgm.%. No significant variation occurred either with or without premedication. Potter et al., Surgery, 10: 757 (Nov.) 1941.

Convulsions occurred when temperature in operating room was 90 to 105°F. as dry and 80-90°F. as wet. Treatment: head elevated about eight inches, ice applied to it, neck and medulla region; firm pressure over carotid for three seconds and repeated once or twice. Calcium gluconate 10% was administered intravenously, at first appearance of twitching. If patient's color was pink, carbon dioxide was given; if there was cyanosis, both carbon dioxide and oxygen were administered. Madan, Brit. M. J., II: 890 (Dec. 20) 1941.

Convulsions: Treatment with 5-6 ml., 2.5% sodium ethyl thiobarbiturate given intravenously effected abrupt cessation. Tye, South. M. J., 35: 339 (Apr.) 1942.

Uterine Contractions in Labor: Open drop method first abolished tonus, then contractions. 30 minutes were required for uterus to regain motility. Bickers, Virginia M. Monthly, 69: 15 (Jan.) 1942.

Intravenous Anesthesia. 200-300 ml. isotonic serum solution containing 4.5-5% was given rapidly, followed by slow intravenous drip to a total of 700 to 800 ml. in an operation of one hour; used in conjunction with pentothal or cyclopropane; 1.0-1.5 liter when used with nitrous oxide and two or more liters when used alone. Preferred method when the patient was dehydrated, weakened, hypotensive or in shock. **Unfavorable Effects:** thrombosis in utilized vein in 25% and albuminuria in 40% of the cases. **Contraindications:** hypertension, plethora, arteriosclerosis, myocardia, albuminuria, edema and hepatic lesions. Hudon and Paradis, Laval méd., 10: 633 (Nov.) 1945.

Corneal Diseases. Satisfactory results were obtained with repeated topical applications in 25 cases of keratitis (herpetic six, disciform four, recurrent erosions three, traumatic six, ulcer one, corneal erosion one, ulcerative pannus four). Kalfa, Věstník Oft., 22: 23, 1913, part 2; Am. J. Ophth., 27: 306 (Mar.) 1944.

Hemoglobin Concentration: 96.2-114% (average of 102.4%) in 15 men with ether anesthesia (eight men showed no increase and three showed decrease). Pender and Lundy, Anesthesiology, 5: 63 (Mar.) 1944.

ETHYL SUCCINATE

Guinea Pigs—

Tuberculosis: Subcutaneously, 0.5 ml. with 0.5 ml. olive oil twice weekly for two to eight weeks inhibited tuberculosis development. Doses of 0.05-0.1 ml. when given alone had no aggravating or retarding effect on the tuberculosis. Berthelot, Nègre, and Bretcy, Ann. Inst. Pasteur, 71: 93 (Mar.-Apr.) 1915.

ETHYL NOR-SUPRARENIN

(1-(3,4-dihydroxyphenyl) 2-amino-1-butanol hydrochloride)

Mice (white)—

LD₅₀: 117 ± 1.01 mgm/kg. intravenously (i.e., 1/120 that of epinephrine). Tainter et al., J. Pharmacol. & Exper. Therap., 81: 269 (July) 1911.

Man—

Diastolic Blood Pressure Decreased: 1–5 minutes after parenteral use of 0.5–2 mgm. doses, effect persisted from 20 to 60 minutes. Pulse rate increased. Ibid.

ETHYLENE CHLORIDE

(1,2 dichloroethane)

Rabbits, Guinea Pigs, Rats, Mice—

Inhalation: 12.4 mgm/liter (3,000 parts per million) for seven hours was fatal. Death preceded by dyspnea and increasing weakness. Pulmonary congestion, mild to moderate degeneration of renal tubular epithelium and occasional necrosis of adrenal cortex. Heppel et al., J. Pharmacol. & Exper. Therap., 84: 53 (May) 1945.

Mice, Rats, Guinea Pigs, Rabbits, Hogs, Dogs—

Toxicity: 6.4 mgm/liter (1,500 parts per million). Almost all animals succumbed before six exposures of seven hours each were completed. Ibid.

ETHYLENE CHLOROHYDRIN**Rats—**

Toxicity: M.L.D. was 5–6 mgm/100 gm. intraperitoneally, and 7–8 mgm/100 gm. orally. Goldblatt, Brit. J. Indust. Med., 1: 213 (Oct.) 1944; through J. Indust. Hyg. & Toxicol., 27: (abstr.) 91 (May) 1945.

Man—

Skin Absorption: Rapidly fatal. Estimated human fatal dose was not more than 5 ml/kg. Smyth and Carpenter, J. Indust. Hyg. & Toxicol., 27: 93 (Mar.) 1945.

ETHYLENEDIAMINE DERIVATIVES**Mice—**

A long series of ethylenediamine derivatives were prepared and trypanocidal action studied. Correlation between structure of compounds and physiologic action was studied.

Toxicity: Subcutaneously, 10 mgm N-(p-isopropylbenzyl)-(1921F); N-(p-methyl benzyl)-(2156F); N-(p-ethylbenzyl)-(2440RP); or N-(p-n-propylbenzyl)-(1986F). 20 gm. proved toxic, 5 mgm/20 gm. were tolerated. Funke, Bovet, and Montezin, Ann. Inst. Pasteur, 69: 358; 1943.

Trypanocidal Action. 1921F, most active against trypanosomes, caused disappearance of parasites from peripheral blood in 16 hours Ibid.

Guinea Pigs—

Trypanocidal Action: 1921F equally active (above) against *T. brucei*. Ibid.

1-N-ETHYLEPHEDRINE HYDROCHLORIDE

(Nethamine)

Rabbits—

Toxicity: Intravenously, 50 mgm killed one out of 12 rabbits. No tissue injury by intravenous or oral dose of 25 mgm. daily or 50 mgm/kg. orally for four weeks. Becker et al., *J Pharmacol. & Exper Therap.*, 75: 289 (Aug.) 1942.

EVIPAL

(5-cyclohexenyl-1,5-dimethylbarbituric acid)

Man—

Obstetrics: 1.0 gm/30 ml. water by rectum and scopolamine, 0.0001 gm., hypodermically were given after start of labor to 66 primigravidae and 28 multigravidae cases with good results in 70%, fair in 11% and poor in 16%. Analgesia in five to ten minutes after administration lasted from two to six hours. Thomas and Taylor, *J Connecticut M. Soc.*, 6: 327 (May) 1912.

FERROUS ASCORBATE**Man—**

Excretion: Intravenously, 30-40 mgm. iron as ferrous ascorbate in physiologic saline caused no increase in fecal iron in two subjects with normal iron reserves, one subject excreted 0.015 mgm. iron in the urine daily. Injection of 30 mgm caused excretion of 0.29 mgm. iron in the urine daily in another subject, more than 65% of the total being excreted within the first 90 minutes after injection. Little, Power, and Wakefield, *Ann. Int. Med.*, 23: 627 (Oct.) 1945

FERROUS SULFATE**Man—**

Microcytic Hypochromic Anemia in Pregnancy 0.4 gm. twice a day was effective. Edwards, *Indian M. Research Mem.*, 33: 1 (Dec.) 1911.

Thoracoplasty Cases. Routine administration of 0.1 gm. three times a day after meals and at bedtime and 1 gm. brewer's yeast. Antianemic therapy gave high hemoglobin per cent Brauerman, *Am. Rev. Tuberc.*, 46: 27 (July) 1912.

Anemia Therapy 0.2 gm a day five days a week for three to six months to children produced significant rise in hemoglobin levels. 27 children with 80% hemoglobin levels showed 10-15% rise after six months of 0.4 gm. of the drug Davidson and Donaldson, *Brit. M. J.*, 1: 76 (Jan) 1911.

Hodgkin's Disease: 0.65 gm. a day plus liver and vitamins increased hemoglobin from 10.4 gm. to 12.6 gm/100 ml. in two weeks. Isaacs, M. Clin. North America, 201 (Jan.) 1944.

Thrombocytopenia Purpura: Administration of iron indicated for anemia, e.g., 1 gm. ferrous sulfate per day; 3 gm. of reduced iron per day, or iron and ammonium citrate, 6 gm. per day. Limarzi, M. Clin. North America, 153 (Jan.) 1944.

FIBRINOGEN

Cats—

Thermal Shock: 3-4 ml. citrated cat blood, heated to 65° C. for one minute, injected intravenously stopped respiration within two minutes; artificial respiration was of no avail. Heated autogenous plasma produced same effects; homogenized heated plasma had no effect. Edit., J.A.M.A., 121: 596 (Feb. 20) 1943.

Tolerance: Rate of injection affects tolerance. 13 ml. tolerated by injection four days later. Ibid.

FLAVAZOLE

(Sulfathiazole and Proflavine)

Man—

Wound Healing: Dusting 0.5 gm. over an area 40.6 cm. square, with a powder containing two to five parts flavazole, and 98-95 parts sulfathiazole, sterilized 50% of wounds within three days and 75% within one week. McIntosh et al., Lancet, 249: 97; 1945.

FLEA EXTRACT

Man—

Bite Desensitization: Extract of powdered dog and human fleas was given intradermally or subcutaneously in a 1:5000 dilution, 0.4 ml. as the initial dose followed by 0.2 ml. for six injections. McIvor and Cherney, Am. J. Trop. Med., 21: 493; 1941.

FLUORESCCEIN

Man—

Delineation of Burn Injury: Not more than 10 ml. sodium salt given intravenously (transient nausea if given rapidly) no staining of superficial layers indicated third degree burn, mottling suggested second degree Dingwall, Ann. Surg., 118: 427 (Sept.) 1943.

Circulation Time of Extremities. 3 ml. of 20% aqueous sodium fluorescein injected into antecubital vein rather rapidly, after patient had spent ten minutes in room at 32-33° C. Observed time required for dye to reach part under investigation, the end point was greenish yellow fluorescent glow under ultraviolet illumination. Sicher, Proc. Staff Meet. Mayo Clin., 18: 515 (Dec.) 1913.

Chilblain Therapy. Intravenously 2-10 ml., 5% solution every other day improved and sometimes cured chilblain. Pautrier, Schweiz med. Wchnschr., 73: 983 (Aug.) 1943, through Practitioner, 151: 381 (Dec.) 1943.

FLUORIDE, SODIUM

Rats—

Dental Caries: Subcutaneously given sodium fluoride or ingestion of water containing ten parts per million of fluorine increased fluorine content of enamel and dentin, but did not decrease susceptibility to caries. Arnold and McClure, J. Dent. Research, 20: 157 (Oct.) 1941.

Dentin: Subcutaneously, 0.05 to 0.3 ml., 2% solution showed six hours later identical changes in enamel of incisor teeth of rats on normal, high or low calcium phosphorus radio diets. Irving, J. Dent. Research, 22: 417 (Dec.) 1943.

Pigs—

Anthelmintic. 1.0 to 2.0% in daily feed for one to three days to 124 pigs removed 96 to 100% ascarides, 10 to 46% whipworms, 1.0 to 45% nodular worms, and 14 to 100% stomach worms. Toxic effects were marked congestion of lymph glands, hemorrhagic gastroenteritis, nephritis and cirrhosis of liver. 10 to 50 gm. as 4.0 to 5% feed caused severe depression with marked gastroenteritis and congested liver and kidneys. With phenothiazine in ratios of 3:1, 2:1, 7:5, and 1:1 given to 17 pigs as 1.2 to 2.0% daily feed, removed 100 and 12% ascarides and nodular worms, respectively. Habermann, Enzie, and Foster, Am. J. Vet. Research, 6: 131 (July) 1945.

Man—

Dental Caries. With topical application of 1:1000 solution for seven to eight minutes every month for six treatments reduced number of dental caries in treated teeth to approximately one third. Bibby, J. Am. Dent. A., 31: 317 (Mar.) 1911.

Seven to 15 topical applications of 2% solution on teeth for eight weeks in 270 children showed 11.1% less permanent teeth attacked in

two years. Knutson and Armstrong, Pub. Health Rep., 60: 1085 (Sept.) 1945.

Topical application of 1:200 aqueous solution, dried with warm air; three applications at each treatment, repeated six times at weekly intervals prevented tooth decay. Moses, Dental Survey, 21: 1998 (Nov.) 1945.

Exposed Dentin and Alveolar Atrophy: Therapy: 0.07 mgm. as isotonic solution in tooth cavities; 0.012 mgm. as paste applied to dentin surface; 0.35 mgm as paste inserted into root canals. Fatal dose of sodium fluoride was 0.16 gm/kg. Lukomsky, J. Dent. Research, 20: 649; 1941.

FLUORINE

Antidotes—

Aluminum sulfate and calcium hydroxide active; less active were calcium lactate, magnesium hydroxide, and boric acid. Rabbits were killed by sodium fluoride, 500 mgm/kg., but others lived if two parts of aluminum sulfate were mixed with each part of sodium fluoride. Marcovitch and Stanley, J. Pharmacol. & Exper. Therap., 74: 235 (Feb.) 1942.

Mice—

Arsenic Detoxication: 14 of 16 fed arsenic-sugar mixture and drinking water containing potassium fluoride 15 mgm/30 ml. for five days and 10 of 12 fed arsenic and water containing potassium fluoride 30 mgm. per 30 ml. survived. Finerty and Grace, Science, 101: 359 (Apr. 6) 1945.

Rats—

125 parts per million fluorine in food or water reduced incidence of dental caries. 2 parts per million did not inhibit caries. McClure and Arnold, J. Dent. Research, 20: 97 (Apr.) 1941.

Toxicity associated with decrease in bone phosphatase activity. Thyroid and thyrotropic hormone of anterior pituitary enhanced fluorine toxicity. De Eds, Floyd, J. Am. Dent. A., 28: 1804 (Nov.) 1941.

Dental Caries. 20 parts per million in water during pregnancy and lactation followed by 0.1 mgm. per day for 21 days to offspring, reduced the resistance of offspring's teeth to fracture. Norvold and Armstrong, J. Dent. Research, 22: 243 (Aug.) 1943.

Experimental Poisoning. 0.47% calcium added to basal diet containing 0.05% sodium fluoride prolonged survival. Ranganathan, Indian J. M. Research, 32: 233 (Oct.) 1944.

Lambs—

Effect: 3 mgm fluorine per day, in form of rock phosphate, had no detrimental effects on growth or feed consumption. 6 mgm. per day dis-

turbed growth and feed, caused bones to be larger but weaker and increased thyroid gland size in fattening lambs. Hatfield, Shrewsbury, and Doyle, *J. Animal Science*, 1: 131, 1942, through *Vet. Med.*, 38: 77 (Feb.) 1943.

Man—

Dental Caries: Prevented with water supply containing 0.5–1.0 parts per million of fluorine. More than 1.5 parts per million disturbed enamel formation. Bibby et al., *J. Am. Dent. A.*, 32: 350 (Mar.) 1945. 1 part per million in drinking water reduced caries. If it was significantly more than this level, it caused discoloration or dental fluorosis (mottled enamel). Hilliard, *New England J. Med.*, 230: 242 (Feb.) 1944. Orally, tablet containing 3 mgm. calcium fluoride, 30 mgm. ascorbic acid and 400 units vitamin D₂ given daily for six to eight months showed 15% incidence in 155 children; 32% incidence in 130 given 3 mgm. calcium fluoride; and 65% in 227 controls. Strean and Beaudet, *New York State J. Med.*, 45: 2183 (Oct.) 1945.

Toxic Fluorosis: Did not develop in five men given 1.0 mgm. three times a day on five consecutive days weekly for 26 weeks in addition to 0.5–0.9 mgm. per day supplied in diets McClure et al., *J. Indust. Hyg. & Toxicol.*, 27: 159 (June) 1945.

Excretion: 93–101% excreted via urine, feces and perspiration when 3–4 mgm. of fluorine was ingested daily. A positive fluorine balance of 1.2 mgm. occurred when 6.0 mgm. fluorine was consumed. *Ibid*

FOLIC ACID

Rats—

Dietary Granulocytopenia. Cured by oral administration of 25 microgram folic acid for four days. Kornberg, Daft, and Schrell, *Proc. Soc. Exper. Biol. & Med.*, 58: 46 (Jan.) 1945.

Experimental Anemia. 80 micrograms per day counteracted hypochromic anemia produced in rats by administration of 50 mgm. promin or 25 mgm. promizole. Higgins, *Proc. Staff Meet. Mayo Clin.*, 19: 329 (June) 1944.

Man—

Excretion: Average excretion in sweat and urine was 30 micrograms per eight hours and 25 micrograms per 24 hours, respectively by four men receiving 1.06 mgm. folic acid in diet for five days. Johnson, Hamilton, and Mitchell, *J. Biol. Chem.*, 159: 125 (July) 1945.

Leukocytes: Weekly injection of liver fraction containing folic acid for one month to more than one year caused 23 to 130% rise in total

leukocytes; the increase reached a maximum two to two and a half hours after injection. Berry, Spies, and Doan, South. M. J., 38: 590 (Sept.) 1945.

Anemia and Leukopenia: Orally, 5 mgm. daily was of little benefit in five cases of refractory anemia, one with leukopenia and another with neutropenia. Watson et al., Am. J. M. Sc., 210: 463 (Oct.) 1945.

FOLLICULAR HORMONE

Man—

Hypergenitalism in Child: Treatment with 100,000 units parenterally given in ten weeks. Erection decreased; five months later erection disappeared and emission was absent. McKenna, Bronstein, and Kiefer, J. Urol., 51: 182 (Feb.) 1944.

FORMALDEHYDE

Man—

Toxicity: No harmful effects if concentrations did not exceed 0.025 mgm/liter or 20 parts per million and if good ventilation existed. Articles with 10% formaldehyde caused cutaneous irritation. Queries and Minor Notes, J.A.M.A., 117: 1834; 1941.

Determination: Formaldehyde in air collected by use of impinger with solution of 1.25% potassium hydroxide. Analysis was made by 1) dropping mercury electrode, 2) color formed with phenylhydrazine hydrochloride and potassium ferricyanide. Barnes and Speicher, J. Indust. Hyg. & Toxicol., 24: 10 (Jan.) 1942.

Plantar Warts: Treated with 3% aqueous solution of formalin, caused pain to disappear in seven to ten days in 39 patients. Warts were scraped away at the end of three weeks. Thomson, Brit. J. Dermat., 55: 267 (Nov.) 1943.

FORMOGUANAMINE

(Diamino-s-triazine)

Rats—

Diuretic Action Was 347 times that of urea. The animals tolerated 2.234 millimols per kg. Useful dosage range was from 0.023–0.09 millimols per kg. orally. Lipschitz and Stokey, J. Pharmacol. & Exper. Therap., 83: 235 (Apr.) 1945.

Dogs—

Diuretic Action: Was 145 times that of urea. Diuresis was maximum in one to three hours, returning to normal in four to six hours after administration. Ibid.

FUADIN

Mice (white)—

Experimental Histoplasmosis Intraperitoneally, 0.25 ml., 6.3% fuadin daily, starting 24 hours after infection, was of no value. Levy, Am. J. Trop. Med., 23: 211 (May) 1915.

Dogs—

Dirofilaria immitis Intravenously, 2 ml. (6.3% solution) given to each of dogs. Ten to twelve injections with beneficial effect. Abstract: Vet. Med., 37: 301 (July) 1912.

Schistosomiasis japonicum Therapy Dose calculated according to ability to retain drug for reasonable time Tubangui and Aguila, Philippine J. Sc., 75: 69 (May) 1911.

Man—

Tolerance: Intramuscularly, 62.6 ml. of 6.3% solution, given as follows: Initially 0.8 ml., increased gradually to 5 ml. daily then 5 ml. on alternate days nine times. No toxic reactions. Almy and Harper, J.A.M.A., 126: 703 (Nov. 11) 1914.

Vincent's Angina. Intramuscularly, 5 ml. doses of 6.3% solution given daily for six injections plus 25–50 mgm ascorbic acid, three times daily. Smith, South. M. J., 35: 299 (Mar) 1912.

Schistosomiasis Therapy Intramuscularly, slowly in three doses of 1.5, 3.5, and 5.0 ml. respectively on three successive days and followed, if no toxic reaction occurred, by doses of 5 ml. on alternate days until 16 doses were given. U. S. War Dept Tech. Med. Bull., 167, War Med. 397 (June) 1915. Intramuscularly, 1.5 ml., 3.5, 5.0 ml. (1 ml.=8.5 mgm. trivalent antimony) for three consecutive days, followed by 5 ml. every two or three days to a total of 45 ml. *Children*, 0.5 ml. followed by 0.5 ml./10 kg. on second day and thereafter 1 ml./10 kg. every two to three days to eliminate ova from stool *Toxic Reaction* weight loss, joint pain, epigastric pain, nausea and vomiting. Hernandez, Puerto Rico J. Pub. Health Trop. Med., 20: 322 (Mar) 1915. Intramuscularly, 28.5–52 ml. eliminated ova in five patients but improved pulmonary lesions of only one patient. Suarez and Hernández, Puerto Rico J. Pub. Health Trop. Med., 20: 191 (Dec.) 1914.

Creeping eruption of two months duration was treated with intramuscular injections of from 1.5 ml. to 5 ml. per day for six days and resumed seven days later with five daily doses of 7 ml. Rubin, J.A.M.A., 124: 668; 1914. 16 patients showed improvement on fifth intramuscular injection, ten received 40 ml. and six a total of 70 ml. Hunt, U. S. Naval M. Bull., 45: 407 (Sept.) 1915. Intramuscularly, 1.5 ml. followed by 3.5 ml. and sub-

sequent injections of 5 ml. were given on alternate days until 70 ml. had been given. McCorkle, *Canad. M. A. J.*, 53: 355 (Oct.) 1945.

Schistosomiasis japonicum: Intravenously, 1.4, 3.5, and 5 ml. doses administered on three successive days, then 5 ml. on alternate days to a total of 16 doses. *Bull. U. S. Army M. Dept.*, 4: 178 (Aug.) 1945.

Urinary Schistosomiasis: Intramuscularly or intravenously, 1 ml. initially, increased to 5 ml. on alternate days until a total of 40 ml. was reached. Peters, Huntress and Porter, *J. Urol.*, 54: 301 (Sept.) 1945.

Cutaneous Schistosomiasis: 40 or 50 ml. courses were given with two courses of treatment being required to eliminate the skin infestation in all cases. Black, *Brit. M. J.* II: 453 (Oct.) 1945.

Bilharziasis of the Bladder: Intramuscularly, 5.0 ml. doses on alternate days were administered after the first two injections of 1.5 and 3.0 ml. on successive days until a total of 40 ml. was given in 16 days. Another 15 day course was given after a rest of 30 days. Ockuly, *J. Urol.*, 54: 39 (July) 1945.

Granuloma inguinale: Consecutive 1.5, 3.5, and 5 ml. doses of 6.4% solution followed by 5 ml. two to three times weekly until cured and then 5 ml. weekly given for six months. If the patient did not respond in six weeks a 1% solution of antimony potassium tartrate was substituted. *Bull. U. S. Army M. Dept.*, 4: 325 (Sept.) 1945.

FUMIGACIN

In Vitro Bacteriostatic—

60–80 mgm/liter for *Staphylococcus aureus*, 20–30 mgm/liter for *Staphylococcus albus*, 25 mgm/liter for *Staphylococcus citreus*, 100 mgm/liter for *Micrococcus tetragenus*, 10–40 for *Streptococcus hemolyticus*, 625 for *Streptococcus viridans*, 15 for *Bacillus anthracis*, 2500 for *Bacillus subtilis*, 625 for non-hemolytic streptococcus. Minzel, Winsteiner, and Hoogerheide, *J. Biol. Chem.*, 152: 419 (Feb.) 1944.

Mice—

Toxicity: LD₅₀, intraperitoneally, 8 mgm. for 20 gm. mice or 400 mgm/kg. of 1% fumigacin dissolved in aqueous 0.05% sodium carbonate. *Protection*: 0.5–2 mgm. retarded death, and several such doses twice daily for two or three days sometimes prevented death after injection of ten to 100 times LD of *Streptococcus hemolyticus*. *Ibid.*

GALACTOSE

Chicks—

Poisoning: 54.6% galactose in diet caused violent spasms and death within a few days. Blood galactose was high, but blood glucose was nor-

mal during spasms. Muscular glycogen was nearly zero. *Dam, Proc. Soc. Exper. Biol. & Med.*, 55: 57 (Jan.) 1944.

GAMMEXANE

(γ -isomer of hexachlorocyclohexane)

Weevils (grain)—

Toxicity: 0.4 parts per million (on weight of the grain) gave a 50% mortality in five days. *Slade, Chemistry & Industry*, Pg. 314 (Oct.) 1945.

Flies (house)—

Toxicity: 0.01% spray killed 73% while 0.02% D D T killed 51%. *Ibid.*

Goldfish—

Toxicity: 1 part per million was definitely harmful. *Ibid.*

Rats—

Toxicity: Ingestion of 10–30 mgm daily for five weeks. Subcutaneously, 100 mgm/kg. killed 25% of the animals, survivors recovered in three days. *Ibid.*

GELATIN

Man—

Retention: Average was 43 1%, and as low as 12.8%, after single intravenous administration of 400–800 ml. of 8% solution in physiologic saline. *Brunschwig et al., Surgery*, 16: 923 (Dec.) 1911

GENTIAN VIOLET

Man—

Eczema Therapy: 0.15 gm. in ointment base was effective. *Ingram, Practitioner*, 147: 700; 1911.

Impetigo: 2% aqueous solution was effective in dry scaly stage. *Smith, Brit. M. J.*, II: 560 (Nov.) 1912.

Oxyuriasis: Orally, 0.064 gm. was given in enteric coated tablets twice daily for eight days. 91% of 1,100 patients responded to three courses of therapy at eight day intervals (total 3.1 gm.). *Peterson and Lahey, J. Lab. & Clin. Med.*, 30: 259 (Mar.) 1915

Oxyuriasis in Children. Enteric coated capsules 0.015–0.06 gm. three times daily for eight days and repeated after rest periods of seven days. *Miller and Einhorn, Am. J. Dis. Child*, 68: 376 (Dec.) 1911

0.5 mgm/kg. per day for three weeks, each week of treatment followed by a rest period of one week. 77% success, considered better than hexyl-resorcinol. *Evans and Moore, J. Pediatr*, 20: 627 (May) 1912.

Enteric coated capsules of gentian violet used. Six 0.03 gm. tablets daily for seven days for persons over 15 years of age were repeated after one week of rest. Children under two were given one or two 0.01 gm. tablets; and older children, doses according to age. Sisk, North Carolina M. J., 5: 52 (Feb.) 1944.

Schistosomiasis: 0.06 gm. enteric coated tablet one hour before each meal until 6 gm. were taken. Not effective on ova. Hernández, Porto Rico J. Public Health Trop. Med., 19: 666 (June) 1944.

Strongyloidosis: 0.03 gm. gentian violet or crystal violet for 8-16 days gave marked improvement in 29 patients. Shikhobalova and Semenova, Klin. med., 20: 5 (76) 1942, through Trop. Dis. Bull. 41: 411 (May) 1944.

GERMICIDES

(Evaluation of)

In Vivo Methods—

Tail of animal was contaminated with virulent organism, treated with disinfectant, and then inserted into peritoneal cavity, and observed for infection. Kempf and Nungester, J. Bact., 43: 49 (Jan.) 1942.

Mice (white)—

Evaluation: Removing a piece of skin, previously infected with *Streptococcus pyogenes* and subsequently treated with a germicidal substance, from the abdominal wall after inserting into peritoneal cavity of same animal and the resulting peritonitis was noted. Sarber, J. Bact., 43: 50 (Jan.) 1942.

GLIOTOXIN

In Vitro—

Bactericidal: 2.5 to 10 micrograms per ml. of agar medium inhibited growth of *Staphylococcus aureus* and *albus* and *Streptococcus viridans* 10 micrograms per ml. agar stopped growth of all gram-negative bacteria Dutcher, J. Bact., 42: 815 (Dec.) 1941.

Toxicity: 50-75 mgm/kg. was toxic in higher animals. Ibid.

Fungistatic Action: 0.1-0.5 mgm. added to 5 ml. culture of *C. albicans* caused free growth after initial inhibition; 2.5 mgm/5 ml. prevented all growth. Reilly, Schatz and Waksman, J. Bact., 49: 585 (June) 1945.

GLOBULIN, GAMMA

Man—

Infectious Hepatitis: Prevention or attenuation by administration of 0.3 ml/kg. body weight, intramuscularly Stokes and Keefe, J.A.M.A., 127: 144; 1945.

Infectious Hepatitis: Intramuscularly, in 5, 8, or 10 ml. doses according to body weight, prevented development of disease. Havens and Paul, J.A.M.A., 129: 270; 1945.

Infectious Hepatitis: Intramuscularly, 0.6 ml/kg. had no demonstrable effect on the incidence, severity, and duration of the disease Gellis et al., J.A.M.A., 128: 1158, 1945.

Preparalytic Poliomyelitis Intramuscularly, 20-100 ml. had no significant effect on muscular involvement. Average amount injected was 84 ml. Bahlke and Perkins, J. Bact., 50: 121 (July) 1945.

Mumps Orchitis: Intramuscularly, 20 ml., prepared from convalescent serum, given to 51 patients in the first 24 hours of parotitis, reduced the incidence from 27.4% for controls to 7.8%. Gellis, McGuinness, and Peters, Am. J. M. Sc., 210: 661 (Nov.) 1945.

Post-transfusion Hepatitis: Injection of 10 ml., repeated one month later prevented the disease in all but 1.3% of 384 (developed in 8.9% of 384 controls). Grossman, Stewart, and Stokes, J. A.M.A., 129: 991; 1945.

GLOBULIN, IMMUNE

Man--

Measles: Intramuscularly, 8 ml. measles antibody was not found efficient for prevention or modification of measles in boys. Gallagher, Am. J. M. Sc., 203: 880 (June) 1942.

GLOBULIN, PLASMA

Man--

Hemophilia: Intravenously or intramuscularly, 11.5 mgm. or more of normal human plasma fraction reduced the coagulation time to near normal in 15 of 16. 200-600 mgm. had an effect equal to that obtained by 80 ml. of fresh plasma or 100 ml. of whole blood. Minot et al., J. Clin. Investigation, 24: 701 (Sept.) 1945.

GLUCOSE

Man--

Fibrositis Therapy 1.5-2 ml. isotonic solution infiltrated into tender spots, three times. Ray, Brit. M. J., II: 850; 1941.

Insulin Coma. Prolonged by maintaining blood glucose at 35 mgm. per 100 ml. by intravenous injection of 5% glucose in physiologic saline at 3-10 ml. per minute. Wortis and Karr, Proc. Soc. Exper. Biol. & Med., 49: 128; 1942.

Rectal Absorption. Less than 1 gm. per hour of isotonic or hypertonic solutions was absorbed. Garrer et al., Acta med. Scandinav., 107: 1, 1911.

Intravenous Glucose: Assimilation rate depended on rate of injection; maximum was 5.77 kg. per hour. Cain and Belk, Am. J. M. Sc., 203: 359; 1942.

Skin Sugar Levels: Normal average was 58 mgm/100 gm. skin; levels exceeding 68 mgm. were pathologic (and responded to diabetic management). Urbach, J.A.M.A., 129: 438; 1945.

GLYCEROL

Rabbits (albino)—

M.L.D.: Intraperitoneally, 7 ml/kg.; subcutaneously, 10 ml/kg.; orally, 14 ml/kg. Repeated and extensive application without toxicity.

Lethal subcutaneous doses caused great reduction of red and white blood cells and hemoglobin content. Injection into heart decreased red cells and hemoglobin content of blood and slightly increased the white cells. Intraperitoneal injections increased white cells. Deichmann, Indust. Hyg. Sect. 2: 5 of Indust. Med., 10: #1 (Jan.) 1941.

GLYCINE

Chicks—

Requirement: Was 1.5% of diet when provided as free glycine, 1.0% when provided in combination as gelatin, edestin, casein, and glycylglycine. Almquist and Mecchi, Proc. Soc. Exper. Biol. & Med., 49: 541 (Apr.) 1942.

Infants—

Respiratory Metabolism: Orally, 1 gm. glycine per kg. increased heat production and nitrogen excretion. Phenylalanine and tyrosine 0.4–2 gm/kg. orally did not produce these effects. Dann et al., Am. J. Dis. Child., 63: 900 (May) 1942.

GLYCOCOL

Man—

Effect on Beri-beri: 10–30 gm. in aqueous solution daily for three to 22 weeks caused gradual recovery from sensory and motor paralysis of extremities after one to two weeks. Kikuchi, J. Osaka Med. A., 40: 801; 1941; through Far Eastern Sci. Bull., 1: 61 (Nov.) 1941.

GOLD

Man—

Dermatitis: Caused by bi-weekly injections of a gold compound over four to five weeks (erythema, exfoliation). Spectrograph revealed 0.5

microgram in affected skin (left thigh), 0.15 microgram/gm. in blood. Ludy and Thomas, Arch. Dermat. & Syph., 49: 365 (May) 1914.

Rheumatoid Arthritis: Intramuscularly or subcutaneously, 25-100 mgm. weekly of gold sodium thiomalate (Myochrysine), gold thioglucose in ascending amounts starting with 10 mgm. twice weekly until 1.2 gm. were given in 21 intramuscular injections, and gold sodium thiosulfate, intravenously in 30 mgm. doses, gave good results. Price, Harper Hosp. Bull. (Detroit, Mich.), 1: 192 (June) 1942.

53% improved with intramuscular injection of 5 mgm. gold thioglucose twice weekly for three weeks, 10 mgm. twice weekly for three weeks, then 25 mgm. once weekly for four weeks, with increase thereafter of 5 mgm. twice weekly to a maximum of 50 mgm. weekly, continued indefinitely or for at least one year. Old persons and those with severe arthritis received 2-3, 5, and 10 mgm. respectively twice weekly during first, second, and third month, then 25 mgm. weekly as tolerated. Rawls et al., Am. J. M. Sc., 207: 528 (Apr.) 1944.

Rheumatoid Arthritis, Chronic: Therapy consisted of weekly intramuscular injections of sodium aurothiomalate. Initial dose of 10 mgm., gradually increased to 100 mgm. until 1 gm. was given. 41% showed marked improvement (of 68 patients), 31% moderate improvement, 17% no improvement. Toxic reactions appeared in 40%, dermatitis being most frequent. Wainwright and Brown, Bull. Johns Hopkins Hosp., 69: 578 (Dec.) 1941.

GOLD SODIUM THIOSULFATE, THIOMALATE

Rats—

Tolerance Development. M.L.D. of gold sodium sulfate was 35 mgm. per kg. intramuscularly. Surviving animals given four doses, tolerated 150 mgm/kg., an increase of 200%. Rats given chronic doses of gold sodium thiomalate survived 100 mgm/kg. (fatal dose) of gold sodium thiosulfate and similarly rats given chronic doses of gold sodium thiosulfate, survived 185 mgm/kg. (fatal dose) of gold sodium thiomalate. Cortell, Proc. Soc. Exper. Biol. & Med., 19: 121, 1942.

GONADOTROPIC EXTRACT

Man—

Tolerated in Pregnancy: Total dose 97.5 gm. without untoward effects (sheep pituitary). Davis & Hellbaum, J. Clin. Endocrin., 1: 100 (Aug.) 1941.

GONADOTROPIN

Mares—

Untreated mare serum collected at 70th day of pregnancy containing 200 international units per ml. Mares given 1,000 international units in single subcutaneous dose; 7 of 9 had conception, estrus induced in 2. Cameron, J. Am. Vet. Med. A., 100: 60 (Jan.) 1942.

Bulls—

Sterility overcome by 2 ml. intramuscular injection of pregnancy urine extract given twice. Ibid.

Man—

Assay: Hormone from urine of pregnant women assayed: 8,000 international units per mgm. Lundgren et al., J. Biol. Chem., 142: 367; 1942.

Synergism of chorionic gonadotropin and pituitary extract injections given three times weekly for 20 days each month for six months, for amenorrhea therapy. Mezer and Ravetz, Am. J. Obstet. Gynec., 41: 474 (Mar.) 1941.

GONADOTROPIN, EQUINE

Man—

Endocrine Sterility in Women: Intramuscularly, 400–800 international units given for ten days, beginning at end of bleeding, followed immediately with intramuscular 500–1000 international units daily for ten days of chorionic gonadotropin. If ovarian failure was due to gametopathic factor, 0.3 mgm. estradiol benzoate every other day for ten days, then 0.3 mgm. estradiol benzoate and 5 mgm. progesterone every other day for ten days were given. Hamblen, North Carolina M. J., 3: 278 (June) 1942.

Delayed Menstruation: 200 international units serum gonadotropic hormone alone or in combination with 100 international units urine gonadotropic hormone given every third day for five injections at the onset of the period is likely to be effective when given over three menstrual cycles at time corresponding to preovulatory phase. MacGregor, Edinburgh M. J., 51: 39 (Jan.) 1944.

Menstruation: Intramuscularly, 200, 400, and 600 international units equine gonadotropin and intravenously, 800 international units given at two or three day intervals were ineffective. Abarbanel and Leatham, Am. J. Obst. & Gynec., 50: 262 (Sept.) 1945.

Hypo-ovarianism Therapy: Intramuscularly, 400 international units daily from the fifth through the 14th day of the cycle and 500 units chori-

onic gonadotropin daily from the 15th through the 25th day were given. Hamblen and Davis, *Am. J. Obst. & Gynec.*, 50: 137 (Aug.) 1915.

Cryptorchid Testes: Intramuscularly, 100 units chorionic gonadotropin given three times a week seven to eight weeks caused descent in 25%. If no response occurred, 200 units given subcutaneously after six months caused descent or localized pain guiding surgeon. Frank, *Am. J. Obst. & Gynec.*, 47: 561 (Apr.) 1944.

Infertility Therapy: 150 units gonadotropic factor given twice weekly alternately with 500 units chorionic gonadotropin twice weekly rendered 273 of 600 fertile. Belt, *M. Ann. District of Columbia*, 14: 450 (Oct.) 1945.

GONOCOCCUS VACCINE

Man—

Gonorrhea Therapy. Sulfonamide resistant patients were treated with a merthiolate preserved vaccine containing four million organisms per 0.1 ml. prepared from resistant and from susceptible strains of the gonococcus. Initial intradermal injection of 0.01 ml. doubled next day if no untoward reactions occurred, succeeding subcutaneous injection being increased from 0.02 ml. to 0.18 ml. for tenth injection. Sulfathiazole administration begun with fifth injection at 4 gm. daily for seven days. Cohn et al., *Am. J. Syph., Gonorr. & Ven. Dis.*, 28: 179 (Mar) 1944.

GRAMICIDIN

Mice—

Acute Toxicity: LD₅₀ was 1.5 mgm/kg of 1% solution in propylene glycol, given intravenously. Anderson et al., *Science*, 103: 419 (Apr. 5) 1946.

Protective Dose. Intra-abdominally, 0.001–0.002 mgm. protected against 10,000 fatal doses of streptococci or pneumococci. Dubos, *New York Acad. Med.*, 17: 405 (June) 1941.

Mice (Swiss)—

Acute Toxicity: Intravenously, LD₁₀₀ was 3.75 mgm/kg on seventh day and 5.0 mgm/kg. within 24 hours, when tested in dose range of 0.625–15.00 mgm/kg. Intraperitoneal toxicity tests with 5–75 mgm/kg. doses produced 100% mortality on seventh day with 60 mgm/kg. No oral toxicity for doses as large as 1000 mgm/kg. Toxic signs were restlessness, followed by depression, and death due to respiratory failure. Robinson and Molitor, *J. Pharmacol. & Exper. Therap.*, 74: 75 (Jan) 1912.

Rats—

Toxicity: LD was 20 mgm/kg. and 450 mgm/kg. for formaldehyde treated gramicidin. 50% hemolysis of rat red blood cells in 40 minutes was caused by 0.05 parts per million and 0.6 parts per million for formaldehyde treated substance. Lewis et al., *Science*, 102: 274 (Sept. 14) 1915.

Rabbits—

Local Reaction: 500 micrograms per ml. of saline applied to cornea for 120 minutes showed no irritation. Dusted into eye sac edema and inflammation of conjunctiva was followed by cloudiness of cornea. Robinson and Molitor, *J. Pharmacol. & Exper. Therap.*, 74: 75 (Jan.) 1912.

Cats—

Blood Pressure: Marked fall after second or third consecutive injection of 1 mgm/kg. while single injections had no such effect. *Ibid.*

Dogs—

Cumulative Toxicity: Daily doses of 2 mgm/kg. caused death after two or three injections. *Ibid.*

GRAMICIDIN-S**Rats—**

M.T.D.: 15–20 mgm/kg. intraperitoneally. Gause and Brazhnikova, *War Med.*, 6: 180 (Sept.) 1944.

Man—

Empyema: 50–100 ml. aqueous solution (4% alcohol diluted with water to give 400–800 gamma/ml.) introduced three times daily after pus evacuation produced prompt response with good tolerance. Toxicity was similar to thyrothycin. *Ibid.*

Locally: *Solutions* for wound irrigation, moist dressings containing 2.0 gm/100 ml. (96% alcohol) dissolving 2–3 ml. of this solution in 500 ml. water. Daily dressings or more frequently plus 15–25 ml. irrigations through Carrel drains or rubber tubes. *Ointments*—3 ml. of 2% alcoholic solution in 100 gm. petrolatum. *Emulsions*—3 ml. of 2% alcoholic solutions in mixture of 100 ml. castor oil.

Toxicity: Used locally as above, nil. Manevitch et al., *Am. Rev. Soviet Med.*, 2: 143 (Dec.) 1944.

HELIUM-OXYGEN**Man—**

Asthma: In severe cases in amounts of six liters of 80% helium and 20% oxygen and reduced as spasm was relieved. Cases which did not respond to other therapy were anesthetized with ether given rectally in olive oil. Peters, *Illinois M. J.*, 82: 428 (Dec.) 1942.

HELLEBRIN

Cats—

LD: 0.1 mgm/kg. intravenously, 10 mgm/kg. orally. Karrer, Helvet. Chim. acta, 26: 1353; 1943, through Chem Abstr., 38: 2960, 1944.

HEMOSTYPHIN

(Lipoid of animal origin)

In Vitro—

Coagulation Time. Minimum dose of 0.005 mgm/ml. shortened time of rabbit's blood. Ruttink, Arch. internat. de pharmacodyn. et de therap., 67: 305 (Apr.) 1942.

Rabbits—

Toxicity: 1 gm/kg. intravenously killed seven of 34. Ibid

HEPARIN

Comparison of Heparins: Isolated in form of crystalline barium salts from dog, beef, pork, and sheep tissue showed anticoagulation potencies in order 10:5:2:1. Chemical differences have not been detected. Jaques, Waters, and Charles, J. Biol. Chem., 144: 229 (June) 1942.

Mice—

Excretion: Appeared in urine one hour after subcutaneous injection of 200–1,000 units. Copley, Science, 93: 478 (May 16) 1941.

Rabbits—

Experimental Venous Thrombosis. 10 mgm in 10 ml saline injected into ear veins, jugular vein traumatized, lumen constricted with loose ligature and wound closed. Thrombus formation prevented if heparin were given before traumatization, and effect enhanced by injections before and after (10 mgm. twice daily for two to five days) injury. Rabinovitch and Pines, Surgery, 14: 669 (Nov.) 1943.

Leukopenia: Within three or four minutes of intravenous dose of 0–12 mgm/kg., transitory leukopenia occurred (normally in six to ten minutes). Rapid administration increased severity. Jucker, Klin. Wchnschr., 22: 221 (Mar. 13) 1943.

Liberation by Trypsin. 3–7 mgm of trypsin per kg. intravenously produced incoagulability, which was not caused by addition of same amount in vitro. Rocha e Silva and Dragstedt, Proc. Soc. Exper. Biol. & Med., 48: 152 (Oct.) 1941.

Toxicity. Intravenously, 10 mgm/kg. four times daily for ten days produced no pathologic changes Joirpes, Acta med. Scandinav., 107: 107; 1941.

Dogs—

Excretion: Appeared in urine one hour after intravenous injection of 100–200 units. Copley, Science, 93: 478 (May 16) 1941.

Liberation by Trypsin: 1–2 mgm. of trypsin per kg., intravenously produced incoagulability of blood not caused by addition of same amount *in vitro*. Rocha e Silva and Dragstedt, Proc. Soc. Exper. Biol. & Med., 48: 152 (Oct.) 1941.

Man—

Adhesion Prevention: Used only in acute partial or complete intestinal obstruction due to adhesions, especially after previous operation for obstruction or repeated attacks. *Contraindicated* when oozing peritoneum after adhesions divided, granulation or subacute inflammation of tissues. *Dose:* 10,000 units/300 ml. physiologic saline, run by gravity into peritoneal cavity through catheter in small stab wound after closure of abdominal wound and additional 5,000 units at 12 hour intervals for three days. Lehman and Boys, Arch. Surg., 43: 933 (Dec.) 1941.

Clinical Use: 1,000 units per hour intravenously, followed by 3–4 ml. undiluted heparin every three hours for an average of seven to nine days. *Complications:* Edema from excessive saline, and bleeding from operative wounds. Value in therapy of postoperative thromboembolic manifestations and in vascular surgery. Lam, West Virginia M. J., 38: 215 (June) 1942.

Leukopenia: As in rabbits, but larger doses required. (See rabbits.)

Method: Administration subcutaneously in Pitkin menstruum containing gelatin, glacial acetic acid, glucose and water to which has been added epinephrine hydrochloride, ephedrine sulfate, chlorbutanol and isoamyl-hydrocupreine di-hydrochloride in various proportions. Single dose lasted 24–72 hours. Adequate heparinization for two weeks with 100 mgm., instead of 630 mgm. by fractional method. Loewe, Rosenblatt, and Lederer, Proc. Soc. Exper. Biol. & Med., 50: 53 (May) 1942.

Postoperative Thrombosis and Embolism: Therapy with continuous intravenous heparin in physiologic saline or 5% glucose. Amount of heparin given maintained coagulation time at 15 to 20 minutes. Starting dose of 20 mgm. per hour was satisfactory and then regulated according to individual requirement. Given for a minimum of seven to ten days. Priestly and Barker, Surg. Gynec. & Obst., 75: 193 (Aug.) 1942.

Pulmonary Embolism Therapy: Continuous intravenous drip of heparin in physiologic saline at 15 to 20 drops per minute. Continued for ten to 14 days. (200 mgm./1,000 ml.) Baker and Eddy, Clinics Virginia Mason Hospital (Seattle, Wash.), 20: 65 (Dec.) 1941.

Thrombophlebitis: Constant intravenous drip or intravenously, 2 ml. in 20 ml. saline every four hours. The dosage was controlled by clotting time measured every 12 hours and discontinued when prothrombin percentage dropped to 70-75%. Evans, Connecticut M. J., 8: 71 (Feb.) 1944.

Beeswax Mixture: 200 mgm. finely powdered heparin in 2 ml. of 10% mixture of beeswax in sesame oil. One half was injected into gluteal muscle following injection of procaine hydrochloride. There was a definite rise in blood clotting time, reaching plateau after 24 hours, which could be maintained for seven or more days by repeated injections Bryson, Code, and Judd, Proc. Staff Meet., Mayo Clin., 19: 100 (Feb.) 1914.

Thrombophlebitis: Continuous intravenous drip of 25 drops per minute an average of 300-600 mgm (200 mgm per liter saline) Discontinued in one to four days when used with dicoumarin Glueck, Ohio M. J., 41: 714 (Aug.) 1945.

Evaluation: Method consisted of diluting a centrifuged mixture of toluidine blue and sample with Tyrode solution until color matched that of standard containing 1 ml. toluidine blue and 9 ml. Tyrode solution. Concentration of 0.00-0.08 mgm/ml sample were determined. Trethewie and Melvin, Australian J. Exper. Biol. & Med. Sc., 23: 241 (Sept.) 1945.

Assay: Degree of clot formation was observed at end of three hours, at 37° C. in tubes containing appropriate amounts of heparin solution in citrated (0.4% sodium citrate) beef plasma to which calcium chloride had been added. Standard and unknown solutions were made to contain 5 gammas of heparin per ml. of 0.9% saline. Data in form of logarithms of concentrations and probits of percentage clot formations were plotted to determine "50% clotting concentration." Potency of unknown was estimated by comparing its 50% clotting concentration with that of standard. Foster, J. Lab. & Clin. Med., 27: 820 (Mar.) 1942.

Thrombosis Prevention and Therapy: Continuous intravenous drip of 20 mgm. per hour. Jorpes, Acta med. Scandinav., 107: 107, 1941.

Varicose Vein: Postoperative edema of legs and other complications following sclerosing of varicose veins with sodium ricinoleate was controlled by intravenous heparin, 10,000 units every four hours, starting 24 hours after operation. Pain relieved after first or second injection. Sedwitz, Am. Heart J., 24: 771 (Dec.) 1942.

HEROIN

Man—

Labor: 0.0027 gm repeated 10 within two hours of expected time of

delivery, perineal injection of 1% procaine plus epinephrine, and light nitrous oxide-oxygen anesthesia during second stage of labor in toxic cases. Philpott, *Canad. M. A. J.*, 45: 539 (Dec.) 1911.

Labor: 0.011 gm. was injected when cervix was two to three fingers dilated; 0.0013 gm. when cervix was fully dilated. In a long first stage, additional doses of 0.0013 gm. were given. If the second stage had started when the patient was admitted, 0.001 gm. was given immediately. No supplementary anesthesia was required in most cases. Ross, *Brit. M. J.*, I: 59 (Jan.) 1944.

HESPERIDIN

(Vitamin P)

Guinea Pigs—

Serum Anaphylaxis: 300 gm. animals were sensitized by subcutaneous injections of 0.2 ml. of horse serum from freshly drawn blood. 0.03 ml. horse serum per 100 gm., given intracardially (left ventricle) three weeks later, produced shock. Intraperitoneally, 10 mgm. daily, for 14 days previous, protected animals from anaphylactic shock. There was no protection with doses of 2.5–5.0 mgm. Single doses of 10, 30, and 50 mgm. given 30 minutes previously produced no shock. Hiramatsu, *Japan. J. Dermat. & Urol.*, 49: 301; 1911; through *Far Eastern Sc. Bull.*, 1: 37 (Sept.) 1941.

Man—

Coagulation Time: Subcutaneously, 2 ml. of 2.5% solution daily for two to 21 days increased average coagulation time in children from 3.16 minutes to 3.95 minutes, seven days after injections. Yoshida, *J. Osaka M. A.*, 40: 759; 1911; through *Far Eastern Sc. Bull.*, 2: 5 (Mar.) 1942.

Capillary Fragility. 100 mgm. daily cured abnormal capillary fragility in 12 allergic children. Rapaport and Klein, *J. Pediat.*, 18: 321 (Mar.) 1941.

HEXADIENOL

Rabbits—

Effect. Injection of 2 gm. or 5 gm. doses had no effect. 10 gm. caused two of ten deaths. Subcutaneously, 2 gm. daily for eight weeks had no reaction. Local application of 1 gm. daily on denuded areas caused no injury and did not interfere with wound healing. Koppányi, *J. Am. Pharm. A. (Scient. Ed.)*, 34: 221 (Aug.) 1945.

Cats—

Diaphoretic Action: Intravenously, 150 and 300 mgm/kg. produced sweating without side reactions. Subcutaneously 0.1–0.3 ml. of 33.3% in the foot pads was also effective. *Ibid.*

Man—

Diaphoresis: 1 gm. inunction to skin caused sweating in five to 25 minutes lasting up to 12 hours and easily stopped by washing with alcohol. *Ibid.*

HEXENAL

(5-cyclo-hexenyl-N,5 dimethyl barbituric acid)

Man—

Anesthesia: Intramuscularly, 20 ml 10% solution in distilled water 15 minutes after 10 mgm morphine, was sufficient for all types of operation producing two to 14 hours postoperative sleep without sequelae. Sinichenko, *Khirurgiya*, No 1, 1943, p. 23, through Australian & New Zealand J. Surg., 14: 61 (July) 1943

HEXESTROL

Man—

Menopause Therapy: 1.5–2.0 mgm per injection were given for 11 months. Oral doses ranged from 21–575 mgm Effective in all cases. Ersner, Mann, and Zamostien, *J. Clin Endocrinol.*, 4: 147 (Apr.) 1944.

Lactation Inhibition: Single intramuscular injection of 12.5 mgm. of dipropionate in oil was effective in 66% of 44 mothers. Orally, 10 to 20 mgm., three times a day, produced inhibition in less than three days in 39% and more than three days in 44% of 23 women Prescott and Basden, *Brit. M. J.*, II: 428 (Sept.) 1944.

n-HEXYL CRESOLS

(3 isomers, viz., 4-chloro-6-hexyl-o-cresol, 4-chloro 6-hexyl-m-cresol and 2-chloro-6-hexyl-p cresol)

Mice—

Toxicity on Subcutaneous and Gastric Administration: Unchlorinated meta compound, LD₅₀ 1.8 ml/kg.; chlorinated, 4.0 ml/kg, unchlorinated para compound, LD₅₀ 2.3 ml/kg, chlorinated, 8.6 ml/kg., unchlorinated ortho compound, LD₅₀ 4.0 ml/kg, chlorinated, 4.5 ml/kg Sah and Anderson, *J. A. Chem. Soc.*, 63, 3164 (Nov) 1941.

HEXYLRESORCINOL

Man—

Enterobius vermicularis: 24 mgm/kg per week for five consecutive weeks produced (maximum single dose of 1 gm) 50% success in children Evans and Moore, *J. Pediat*, 20: 627 (May) 1942

Teniasis: 0.4–1.0 gm. cleared five of 19 in one dose and four in two

doses. "Cure" rate 47%. Mukerji and Maplestone, *Indian M. Gaz.*, 78: 283 (June) 1943; through *Trop. Dis. Bull.*, 40: 925 (Dec.) 1943.

Ascariasis: Orally, 0.1 gm. per year of age of patient. A laxative was given 24 hours before and after the vermifuge. Ova disappeared after one course of treatment in 85 patients. Einhorn, Whittier, and Miller, *Am. J. Dis. Child.*, 69: 237 (Apr.) 1945.

Roundworm Therapy: Orally, 0.6–1.0 gm., depending on age, administered in early morning on empty stomach, removed 90–100% ascarids. Andrews, J. M. A. Georgia, 31: 71; 1942.

HIPPURIC ACID

Mice (white)—

LD₅₀: 4.15 ± 0.7 gm/kg. intravenously. Mattis et al., *J. Pharmacol. & Exper. Therap.*, 84: 147 (June) 1945.

HISTAMINASE

Man—

Ivy Dermatitis: Orally, 45 units daily for ten to 25 days effected fair results. Moss, *North Carolina M. J.*, 3: 243 (May) 1942.

Urticaria Therapy: 60–120 histamine detoxifying units daily clinically improved 21 of 35. (1 unit of histaminase capable of detoxifying 1 mgm. histamine in 24 hours at 37° C.) Laymon, *Minnesota Med.*, 25: 466 (June) 1944.

Serum Reaction: Orally, 20 units every three hours for generalized and localized serum reactions, following injection of 1500 units tetanus antitoxin in 15 patients had no effect on duration or intensity of symptoms. Eger and Stone, *Pennsylvania M. J.*, 47: 371 (Jan.) 1941.

HISTAMINE

Guinea Pigs—

In Anaphylactic Shock: Protection by histaminase. Intracardially, 8 ml/kg. histaminase (0.9 units per ml.) did not significantly protect as an equivalent amount of saline did against intraperitoneal dose of 25 mgm/kg. histamine hydrochloride. Hawes, Alles, and Miller, *J. Lab. & Clin. Med.*, 27: 337 (Dec.) 1941.

Maximum Tolerated Dose: Intraperitoneal dose injected as dihydrochloride was less than 2.5 mgm/kg. 4 mgm. histamine per kilo was antidoted by addition of 100 units of histaminase for each mgm. of histamine

hydrochloride in solution before intraperitoneal injection Barlow and Homburger, *J. Allergy*, 12: 346 (May) 1941.

Histamine Shock Prevented in four of seven animals receiving one unit posterior pituitary pressor extract (Pitressin), three hours before receiving a lethal dose (0.66 mgm) of histamine. Subcutaneously, one dog unit of suprarenal cortex extract (Eschatin) plus 10 ml. normal physiologic saline intraperitoneally three hours preceding lethal doses of histamine di-hydrochloride given subcutaneously, delayed histamine shock 0.5 hour in seven animals Wittich, *Ann. Allergy*, 1: 154 (Sept.-Oct.) 1943.

Guinea Pigs, Rabbits, Cats—

Skin Reaction. Intradermally, concentrations graded from 1.0 to 0.0001% histamine diphosphate caused no reaction. Darsie et al., *Proc. Soc. Exper. Biol. & Med.*, 59: 278 (June) 1945.

Rabbits—

Ulcer: Daily injection of 30 mgm in beeswax resulted in presence of free hydrochloric acid which with anemia were etiologic factors of ulcers. Wangenstein, *Canad. M. J.*, 53: 309 (Oct.) 1945.

Dogs—

Tolerance: No tachyphylaxis occurred on subcutaneous injection of 0.01–0.8 mgm. doses as measured by gastric secretory response. Dogs failed to provide experimental analogy for desensitization in allergy. Wells, Gray, and Dragstedt, *J. Allergy*, 13: 77 (Nov.) 1941.

Dogs, Goats, Man—

Skin Reaction: Intradermally, graded concentrations from 1.0 to 0.0001% produced marked whealing, the size increased proportionately with concentration. Darsie et al., *Proc. Soc. Exper. Biol. & Med.*, 59: 278 (June) 1945.

Man—

Headache Therapy. Subcutaneously, 0.25 ml. of solution containing 0.276 mgm. histamine acid phosphate per ml. physiologic saline, increased 0.05 ml. twice a day up to 1 ml. by sixteenth injection and 1 ml. thereafter. Maintenance dose was 1 ml. one to three times a week Shea, *Laryngoscope*, 55: 325 (July) 1945.

Vertigo: 0.5 ml. solution containing 2.75 mgm. histamine acid phosphate in 5 ml. physiologic saline twice a week, controlled vertigo. *Ibid.*

Basal Metabolic Rate Increased by 2.75 mgm. histamine biphosphate in 1:250,000 dilution (30–210 drops per minute). Peters and Horton, *Am. Heart J.*, 27: 845, 1944.

Oxygen Blood Saturation Increased in five persons. For dose see above.

Pheochromocytoma: 0.05 mgm. histamine base intravenously produced typical attack (tentative diagnostic test). Roth and Kvale, Proc. Centr. Soc. Clin. Res., 17: 18; 1944.

Atopic Dermatoses: 26 patients, chronic urticaria, angioneurotic edema, atopic dermatitis, prurigo mitis, generalized pruritis and pruritis ani were treated with 50–175 ml. solution containing 5.5 mgm/500 ml. saline, intravenously, two to four times daily, followed by one or two weeks of 0.02–0.2 ml. of 5.5 mgm. histamine phosphate in 5 ml. saline intradermally or subcutaneously. Best result obtained in chronic urticaria. Toxic reactions avoided when intravenous slow drip method was employed. Smith, Arch. Dermat. & Syph., 44: 883 (Nov.) 1911.

Psychoses: Amounts up to 12 mgm. were effective in 25% of those who failed to respond to insulin-electric shock treatment. Taylor, J. M. Soc. New Jersey, 42: 300 (Sept.) 1945.

Allergic Rhinitis (Perennial): Subcutaneously, histamine phosphate in initial dose from 0.01 to 0.1 microgram and then increased at each dose 50% (highest dose 100 micrograms) was given two or three times a week at beginning and later spaced from five to 21 days apart. Farmer and Kaufman, Laryngoscope, 52: 255 (Apr.) 1942.

Seasonal Allergic Rhinitis: Started eight to ten weeks before pollinating season with 1 microgram initial dose; subsequent doses ranged from two to 75 micrograms at four day intervals and the ninth through fourteenth doses at 100 micrograms at one week intervals. 30 micrograms every week during pollinating season. Ibid.

Gastric Secretion (fasting subjects): Intravenously, seven units of insulin 40 minutes after removal of resting juice, followed in 20 minutes by 0.5 mgm. histamine gave average maximum free concentration of 100–120 ml. N/10 hydrochloric acid per 100 ml. gastric juice and a secretion rate of 2.5–3.5 ml. per minute. Gill, J. Physiol., 102: 13P (Dec.) 1943.

Multiple Sclerosis Therapy: Daily, 2.75 mgm. histamine diphosphate in 250 ml. isotonic sodium chloride were given intravenously, 2 to 6 ml. per minute. Average patient received 40 to 50 injections. Horton et al., J.A.M.A., 124: 800; 1944.

HISTIDINE

Man—

Excretion Rates: Highest excretion occurred in pregnant women between third and eighth month of gestation. Orally, 1 gm. resulted in greater excretion in pregnant than in nonpregnant women. Page, West. J. Surg., 51: 482 (Dec.) 1943.

HISTOPLASMIN

Guinea Pigs—

Cross Reactions: 1:100 dilution gave positive reactions in animals with experimental histoplasmosis, blactomycosis, coccidiomycosis, and haplomyosis. Emmons, Olson, and Eldridge, Pub. Health Rep., 60: 1383 (Nov.) 1915.

HORMONES

Rats—

Greying: 0.25 and 0.5 ml. adrenal cortical extract; 2.5 mgm. desoxy-corticosterone acetate; 1, 5 and 10 mgm. thyroid, 0.25 and 0.5 ml. anterior pituitary extract failed to prevent greying and definite symptoms in piebald animals on vitamin B complex free diet. Mushett and Unna, J. Nutrition, 22: 565 (Dec.) 1911.

Rats (male)—

Antagonistic Activities. Injection of 0.018-0.2 mgm. estradiol dipropionate per week or of 0.09 mgm. estradiol benzoatebutyrate per week for three and a half months produced myofibrous changes in sex organs and cystic degeneration of kidneys. These were prevented or minimized by parenteral administrations of androsterone, transdehydroandrosterone, testosterone or testosterone dipropionate. Korotchevsky, Arch. internat. de pharmacodyn. et de therap., 70: 411 (June) 1915.

Cats, Rabbits, Dogs, Pigs, and Goats—

Average Output (fairly constant for five species), of one adrenal gland per minute per kilo body weight, was determined as equivalent to 0.6 gm. adrenal tissue by comparison of potency of adrenal blood with a commercial extract, Eucortone (1 ml. was equivalent to 75 gm. of gland). Vogt, J. Physiol., 102: 341 (Dec.) 1913.

HORMONES, ADRENAL CORTICAL

Quantitative Bioassay By the muscular work test using adrenalectomized nephrectomized rat. A unit of activity is the work equivalent to a 0.2 mgm. dose of 17 hydroxy 11-dehydrocorticosterone administered twice during the test. Method was specific for the detection and estimation of biologic activity characteristic of C_{21} oxygenated cortical steroids. Ingle, Endocrinology, 34: 191 (Mar.) 1911.

HORMONE, MALE

Man—

Dysmenorrhea 200 mgm. of androgen was given per month with rest periods after each course of 100 mgm. or less. Weinstein, New Orleans M. & S. J., 96: 396 (Mar.) 1911.

HYDROGEN FLUORIDE

Man—

First Aid on Contact: Flush well with water at least ten minutes, apply 10% ammonia; rinse with water; rub a salve containing magnesium oxide and glycerin into the affected area to precipitate the fluorine ion. If acid has penetrated deeply, inject 10% calcium gluconate or 20% magnesium sulfate, hypodermically around and under affected area. Benson, Indust. Med., 13: 113 (Jan.) 1944.

HYDROGEN PEROXIDE

Dogs—

Whipworm Therapy: Rectal injection of 2% solution about 4 ml. to each 4.5 kg. Whitney, Vet. Med., 37: 217; 1942.

HYDROGEN SULFIDE

Man—

Maximum Permissible Concentration: 0.028 mgm. per liter of air at 25° C. and 760 mm. Hg for not more than eight hours daily. Toxicity increased with humidity.

Treatment of Poisoning: Removal to fresh air and rest. In the eye one drop of olive oil and in serious cases three or four drops. 1:1,000 solution epinephrine every five hours if conjunctivitis occurred. Pub. Health Rep., 56: 684 (Apr.) 1941.

HYDROQUINONE AND MONO-METHYL-PARA-AMINOPHENOLSULFATE

Man—

Fatalities: Orally, 15 gm. of a "developing" powder containing above ingredients caused death in two men, 73 and 92 hours later. Both had severe abdominal pain, progressive cyanosis, tachycardia, melena and hematuria. Hemolytic anemia with jaundice. Zeidman and Deutl, Am. J. M. Sc., 210: 328 (Sept.) 1945.

HYDROXYACETIC ACID

Cats—

Continued Administration: Orally, 100 mgm. sodium hydroxyacetate per kg. daily was given without toxic effects. Krop, Gold, and Paterno, J. Am. Pharm. A. (Scient. Ed.), 34: 86 (Mar.) 1945.

Dogs—

Toxicity: 500 mgm/kg. daily for four months was tolerated. Ibid.

IMIDAZOLE

Cats—

Anti-histamine Effect: Intravenously, one and 128 mgm/kg. reduced vaso-depressor action about 25% and 50%, respectively. Morris and Dragstedt, Proc. Soc. Exper. Biol. & Med., 59: 311 (June) 1915.

INDANDIONE DERIVATIVE

(2-isovaleryl-1,3-indandione)

Rats—

Cumulative Toxicity. Subtoxic doses in diet caused death in five to 20 days. Kabat, Stohlman, and Smith, J. Pharmacol. & Exper. Therap., 80: 160 (Feb.) 1914.

Rats and Rabbits—

Acute Toxicity: 200 mgm. caused death in two to twelve hours. Ibid.

INDIGO CARMINE

Man—

Urinary Findings Intravenously, 5 ml. of 0.8% solution caused abnormal changes in urinary sediment, including blue casts, blue mucus shreds and dye crystals in 34 of 80 patients. Douglass and Ransom, J. Urol., 51: 228 (Feb.) 1914.

INDOLE

Dogs—

Effect: Intravenously, 25 mgm/kg. to animals anesthetized with pentobarbital produced a short period of apnea, followed by hyperpnea, an immediate fall in systemic blood pressure, rise in intestinal tone followed by a fall, increase of mucous and salivary secretions, and chronic convulsive movements. Not abolished by atropine. Intravenously, 60 mgm. per kg. caused more intense symptoms without return to normal. Death resulted from continuous fall of blood pressure to zero, attributed to dilatation and arrest of heart action. Ets and Feinberg, Am. J. Physiol., 136: 617 (June) 1912.

INFLUENZA VACCINE

Mice—

Intraperitoneally, two 0.5 ml. doses of a 2×10^2 dilution against 10,000 (50% mortality) doses of type A virus and two 0.5 ml. doses of a 2×10^4 dilution protected them against 1,000 (50% mortality) doses of type B virus. Salk et al., Am. J. Hyg., 42: 307 (Nov.) 1915.

Man—

Effectiveness: Subcutaneously, 1 ml. of virus A and B vaccine four to five weeks before first outbreak produced 3.92% incidence in 457, and 5.97% in 435 controls. Eaton and Meiklejohn, *Am. J. Hyg.*, 42: 28 (July) 1945.

Immunization: Inoculation with 1 ml. containing type A and B virus increased antibody titers in majority of 3914 persons and protected them against an epidemic one year later. Salk et al., *Am. J. Hyg.*, 42: 307 (Nov.) 1945.

Vaccination: Subcutaneously, 1 ml. containing both A and B virus reduced susceptibility to influenza in 599. Rickard, Thigpen, and Crowley, *Am. J. Hyg.*, 42: 12 (July) 1945.

INFLUENZA VIRUS**Chick Embryos—**

Infectivity: A linear relationship with a slope approaching unity existed between log concentration of viral N/ml. of inoculum giving 50% infection and log volume of inoculum when volume was 0.001–1.024 ml Taylor et al., *J. Immunol.*, 48: 191 (Mar.) 1944.

INOSITOL**Mice—**

Alopecia: From basal diet plus 100 mgm. inositol/100 gm. ration was cured by 5 mgm. pantothenic acid/100 gm. ration. Wooley, *Proc. Soc. Exper. Biol. & Med.*, 46: 565: 1941.

Rats—

Alopecia: 3 gm/kg. ration prevented and cured loss of hair and gave a growth response. Cunha et al., *Proc. Soc. Exper. Biol. & Med.*, 54: 236 (Nov.) 1943.

Man—

Cancer of Gastrointestinal Tract 280 mgm. to ten patients was effective in reducing fatty concentration in liver as 8 gm. lipocaic. Abels et al., *Proc. Soc. Exper. Biol. & Med.*, 54: 157 (Oct.) 1943.

INSULIN

Detection in Urine Precipitate by half saturation with ammonium sulfate at pH 5, elute at pH 8, and bioassay of eluate on rabbits. Cutting, *Biochem. J.*, 36: 376 (Apr.) 1942.

High Dosage: 85 units regular and 30 units protamine zinc insulin controls and maintains diabetes mellitus with Albright's syndrome. Peck and Sage, Am. J. M. Sci., 208: 35 (July) 1944.

Infective Hepatitis: Treatment with ten units twice a day, 25 mgm. vitamin C three times a day, and at least 142 gm. glucose daily, continued until urine was free of bile was recommended for those with severe symptoms. Gordon, Brit. M. J., I: 234 (Feb.) 1944.

Insulin Resistance: Overcome by continued use. 50-60 units per day was level of complete diabetes, and normal person was presumed to produce this amount daily. Lerman, Am. J. M. Sc., 207: 354 (Mar.) 1944.

Psychoses: Shock treatment continued for 50 days was best. A dose of 1,000 units had been given, but maximum dose was usually 300 units. Taylor, J. M. Soc., New Jersey, 42: 300 (Sept.) 1945.

Rehabilitation: Initial dose of 30-40 units, subsequently increased each day until physiologic response was obtained, effected improvement in neurotic symptoms and gain in weight of soldiers. Fox, Bull. U. S. Army M. Dept., 4: 447 (Oct.) 1945.

Sedation Therapy: Ten units initially, increased ten units per day to 50 to 90 units relieved anxiety in 19 of 28 patients. (Schizophrenic excitements, panic, catatonic stupors, hebephrenic dilapidation, suicidal depression, etc.) Rennie, Arch. Neurol. & Psychiat., 50: 697 (Dec.) 1943.

Sensitivity: Patient with diabetes given insulin in 1922 and 1936 without reaction exhibited severe urticarial and anaphylactic shock when treatment was resumed in 1940. Reaction to regular protamine zinc and crystal insulin. Patient desensitized by small increasing dose of regular insulin. Higgins, U. S. Naval Med. Bull., 40: 127 (Jan.) 1942

Tolerance: 25 normal (2-22 months) infants, fasting blood sugars average 73.6 mgm.% and average levels 20, 40, 60, and 120 minutes after injection of 0.25 unit regular insulin per kg. body weight gave 55.1, 47.0, 49.2, and 46.2 mgm.% respectively. In 12 infants fasting blood sugars equaled 71.75 mgm.% and averaged levels 30, 60, 90, 120, and 180 minutes after administration of 1.75 gm. glucose per kg. body weight of 126.8, 126.7, 122.8, 98.4, and 75.8 mgm.%, respectively. Daniel, J. Pediat., 19: 789 (Dec.) 1941.

Treatment of Psychoses: 40 units, intravenously and hypoglucemic state should not last more than 0.5-1 hour. Results best in acute psychoses of short duration. Polatin and Spotnitz, Am. J. Psychiat., 99: 394 (Nov.) 1942.

Controlled administration of insulin intramuscularly, and 5% glu-

glucose intravenously, to keep blood sugar at 35 mgm/100 ml. Hypoglycemia for 24 hours and coma for 20 hours without mishap. Wortis, Terris and Karr, *Am. J. Psychiat.*, 99: 391 (Nov.) 1942.

Coma: Produced (shock therapy) by 110-400 units given subcutaneously within 153 minutes and with 110-510 units given intravenously in 85 minutes Revitch, *Phila. Psychiat.*, 52: 83 (July) 1944.

INSULIN, GLOBIN, WITH ZINC

Man--

Description: Sterile solution containing 80 U.S.P. units per ml. 3.6 to 4.0 mgm. globin and 0.25 to 1.5 mgm. total nitrogen per 100 U.S.P. units of insulin. Administered by deep subcutaneous injection, never intramuscularly or intravenously. First dose for patient receiving protamine zinc insulin should not be greater than one-half of total dose of all insulin received on previous day. Council on Pharmacy & Chemistry, *J.A.M.A.*, 124: 838; 1944.

INSULIN, PROTAMINE ZINC

Man--

Diabetes: One daily injection controlled 79% of 611 patients. 77% received 40 units or less daily, 40 to 60 units were given to 64, and 65 to 80 units to 35. Allersberg and Dolger, *J.A.M.A.*, 128: 414, 1915.

Diabetes Therapy Simplified: One unit was given for every 2 gm. of glucose excreted, but not less than ten units per day. If additional crystalline insulin were necessary, not more than one-third of total insulin dose per day was given. Pennock, *J. Lab. & Clin. Med.*, 29: 168 (Feb.) 1944.

INULIN

Dogs--

Effect: Intravenously, 10 to 150 ml. inulin solution in 0.65% sodium chloride caused a marked decrease in red blood cells. Repeated administration over two months caused a progressive drop in red blood cells, but no change in internal organs. Hueper, *Arch. Path.*, 40: 11 (July) 1915.

IODINE

Determination--

Photoelectric Colorimetry: Estimation of microgram quantities in blood using the photoelectric colorimeter in the final step to measure intensity of starch-iodine color and catalytic effect of iodine on ceric-arsenite reaction gave results which compare well with those obtained

with thiosulfate titration. Strickler and Strickler, *Endocrinology*, 37: 220 (Sept.) 1945.

Smith Jaundice Test—

Suspected fluid overlayed in test tube with a small quantity of 0.7% tincture iodine. A distinct green ring formed at juncture, if bile pigments were present. Love and Leake, *U. S. Nav. M. Bull.*, 40: 430 (Apr.) 1942.

Chick Embryos—

Smallest amount causing death was 0.018 gm/kg. Dunham, *Proc. Soc. Exper. Biol. & Med.*, 50: 274 (June) 1942.

Guinea Pigs—

Iodine Metabolism: Potassium iodide, sodium iodide, diiodotyrosine, thyroglobulin, thyroxin, given intraperitoneally in 0.5 microgram iodine per kg. Doses every 72 hours for three doses elevated the mean thyroid and blood iodine. Hinton, Eckerson, and Bruger, *Ann. Surg.*, 115: 206 (Feb.) 1942.

Man—

Allergy: Therapy with several doses of 0.3–0.6 gm. sodium chloride tablets. (Patch test with tincture iodine caused marked reddening and itching six to eight hours later.) Pelner, *J. Lab. & Clin. Med.*, 27: 1150 (June) 1942.

Aspergillus Infection: 4 gm. of iodide daily for 3.5 months produced clinical improvement. Sartory and Sartory, *Compt. rend. Acad. d. sc.*, 216: 426 (Mar.) 1943.

Smallest amount causing death was 0.004–0.019 gm/kg. Dunham, *Proc. Soc. Exper. Biol. & Med.*, 50: 274 (June) 1942.

IDOACETIC ACID

Rats—

Atmospheric Effect: 1 mgm. injected into infant rats which were placed in nitrogen atmosphere 15 minutes later, resulted in death three minutes later. Animals survived for 50 minutes if left in air. Himwich, Fazekas, and Alexander, *Proc. Soc. Exper. Biol. & Med.*, 46: 553 (Apr.) 1941.

Dental Caries: 200 parts per million in food plus 20 parts per million in water reduced dental caries incidence. McClure and Arnold, *J. Dent. Research*, 20: 97 (Apr.) 1941. Injection of 400 parts per million every second day caused 2.2 caries, 200 parts per million given in water, 3.0 caries;

and 200 parts per million in food caused 3.5 caries in desalivated animals. Powell and Dale, J. Dent. Research, 22: 257 (Aug.) 1943.

IODOPHTHALEIN SODIUM

Man—

Effect: Intravenously, 3 gm/70–73 kg. produced a drop in blood pressure. Lawson, Arch. Int. Med., 76: 143 (Sept.) 1945.

IRON

Man—

Absorption of Hemoglobin Iron: Administration of one liter of blood by duodenal tube showed that 10 to 25% iron was absorbed. Black and Powell, Biochem. J., 36: 110 (Feb.) 1942.

Requirement: 0.35 mgm/kg in food was sufficient to maintain normal hemoglobin range of 12 to 14 gm. in children of eight to 11 years. Johnston and Roberts, J. Nutrition, 23: 181 (Feb.) 1942. Average daily intake of 10.44 mgm. caused storage of 1.37 mgm in women of 16 to 27 years. Leverton and Marsh, J. Nutrition, 23: 229 (Mar.) 1942.

IRON, REDUCED

Man—

Iron Deficiency Anemia: 3 gm. daily. Fowler, Clin. Med., 49: 74; 1942.

IRON AND AMMONIUM CITRATE

Man—

Hemoglobin Gain: Blood donors, given 1 gm daily increased average hemoglobin gain from 0.0518 to 0.0772 gm, an increase of 49%, and shortened recovery period from 48.2 days to 35.2 days, a reduction of 26.9%. Fowler and Barer, J. A. M. A., 118: 421; 1942.

Hypochromic Anemia of Pregnancy: 2 gm. three times daily. Hamilton and Wright, Lancet, 213: 184 (Aug.) 1942.

Idiopathic Hypochromic Anemia: 7.8 gm taken daily gave reticulocytosis of 8% a week later, and one month later, patient made complete symptomatic recovery. Currie, Brit. M. J., 1: 762 (June) 1912.

Iron Deficiency Anemia: 6 gm daily of ferric salt. Fowler, Clin. Med., 49: 74; 1942.

Microcytic Hypochromic Anemia of Pregnancy: 1.3 gm ferrous ammonium citrate with glucose twice daily or 2.6 gm iron and ammonium citrate three times daily were taken after meals with a glass of water. Napier and Edwards, Indian M. Research Mem., 33: 1 (Dec.) 1911.

ISONIPECAINE

(Ethyl-1-methyl-4-phenyl-isonipicotate hydrochloride)
(demerol, pethidine)

Mice—

Analgesia: One-sixth to one-fifth as effective as morphine hydrochloride against mild pain stimuli, ineffective against severe pain. Woolfe and MacDonald, J. Pharmacol. & Exper. Therap., 80: 300 (Mar.) 1944.

LD₅₀—147 mgm/kg. intraperitoneally; 221 mgm. orally. Gruber, Hart, and Gruber, J. Pharmacol. & Exper. Therap., 73: 319 (Nov.) 1941.

Rats (albino)—

LD₅₀ 93 mgm/kg., intraperitoneally. Ibid.

Rabbits—

LD₅₀—32 mgm., intravenously, for small animals (1.3–2.4 kg.).

LD₅₀—20 mgm., intravenously, for large animals (2.3–4.2 kg.). Ibid.

Dogs—

Effect: 0.25 mgm/kg., intravenously, caused a fall in blood pressure, respiratory decrease in depth and frequency. Repeated administration caused death from respiratory failure. Ibid.

Man—

Addiction Liability: Abstinence syndrome appeared for two days after ten days substitution for morphine. Increasing doses were given to post-addicts (maximum daily dose 3.5 gm.) for 10–11 weeks. Signs of withdrawal appeared one to two months after administration as typical abstinence syndrome. Himmelsbach, Fed. Proc., 1: 153; 1942.

Analgesic: Never given intravenously nor in a dose >35 mgm. hypodermically if patient were ambulatory. Batterman, Connecticut M. J., 8: 13 (Jan.) 1944. Optimum pain relief with 50–100 mgm. orally or parenterally. Prescott, Brit. M. J., I: 34 (Jan.) 1945. Subcutaneously, 100 mgm., and orally, 50 mgm. Batterman, Arch. Int. Med., 71: 345 (Mar.) 1943.

Effective Analgesic. Orally or intramuscularly, 50–150 mgm. in a single dose or repeated doses several times a day. Effect in 20–60 minutes when given orally, 15 minutes parenterally. Duration two to three hours. Batterman, Fed. Proc., 1: 143, 1942.

Evaluation: Moderate sedative effect inhibited segmental but activated propulsive peristalsis of gut. Analgesic and spasmolytic properties were valuable in asthma, pleuritis, and biliary and ureteral tract spasms. Did not affect blood pressure or blood picture, did not alter blood sugar levels, delayed gastric emptying about 20%, had no cumulative action,

and did not induce habituation. Hoffman, *Anesthesia and Analgesia*, 22: 336 (Nov.-Dec.) 1913.

Gastroscopic Preparation Intramuscularly, 75-150 mgm. 15 to 20 minutes before examination effectively relaxed patient without appreciably affecting blood pressure, pulse rate, or respiration. Huford, *Rev. Gastroenterol.*, 11: 328 (Sept.-Oct.) 1914.

Obstetrics: 100 mgm. intramuscularly was sufficient in 11 patients. Doses repeated to others at two hour intervals. Successful anesthesia obtained in 78.4% of 102 patients. Uterine contractions not retarded, mother or child not harmed, post-partum hemorrhage not induced. Tended to increase incidence of forceps cases. Cripps, Hall, and Haultain, *Brit. M. J.* II. 498 (Oct.) 1914. With scopolamine provided satisfactory amnesia in 70% of 2116 patients, and increased number of babies who breathed immediately, from 62% to 82% using scopolamine instead of barbiturate. Intramuscularly, 100 mgm. (or retention enema containing 8 ml. paraldehyde, 60 ml. ether, and 60 ml. oil) depressed patients who became over-excited with scopolamine. Irving, *Rhode Island M. J.*, 28: 193 (July) 1915.

Respiration. Injection of 100 mgm. into deltoid region of patients with intracranial lesions caused fall in respiration from 18-22 per minute to 4-12 per minute in seven of 20 patients. Guitman, *J. A. M. A.*, 121: 155; 1914.

Surgery: 1,000 administrations without toxic reactions. Not as effective as morphine in 10% but remedied by 100 mgm. given hypodermically or 125-150 mgm. intramuscularly. Demerol had no constipating action. White, *Virginia M. Monthly*, 71: 351 (July) 1914.

Tolerance. Effect of pain threshold determined by initial subcutaneous dose of 100 mgm. All patients took gradually increasing doses at regular intervals, limits of 300 mgm. per dose and a minimum interval of 1.5 hours between doses. Tolerance to ability of drug to raise pain threshold was developed to maximum in eight weeks and maintained for 30 days after drug was discontinued. Andrews, *J. Pharmacol. & Exper. Therap.*, 75: 338 (Aug.) 1912.

Obstetrical Analgesia. Intramuscularly 100 mgm. repeated in one hour with or without chloral bromide opium mixture or 0.1 mgm. scopolamine, or 100 mgm. intravenously followed in one hour by 100 mgm. intramuscularly alone or with 0.1 mgm. scopolamine. With either method, intramuscular injection of 100 mgm. could be given to a total of 100 mgm. in 24 hours. Analgesia was obtained in five to ten minutes intravenously, and 15 minutes intramuscularly. Effect lasted for three to

four hours. Satisfactory relief in 60 of 100 patients, and none in ten of 100 patients. Gallen and Prescott, Brit. M. J., I: 176 (Feb.) 1944. Intramuscularly, 100 mgm. repeated at hour or two to four hourly intervals Brit. M. J., II: 498 (Oct.) 1944.

Orally, 25 mgm. and repeated half an hour later brought best response in first stage of labor. 17.5% were greatly relieved, 72.5% had good relief, and 10% no relief. 25 mgm. dose was effective in 20 to 30 minutes and action lasted one to four hours. Spitzer, Brit. M. J., I: 179 (Feb.) 1944

Morphine Addiction: Reduction from 2.0 to 1.0 gm. of morphine overnight in a 90 year old addict given 100 mgm. Demerol. Massee, J.M.A., Georgia, 34: 154 (Aug.) 1945.

Spasmolytic: 100 mgm., subcutaneously promptly relieved status asthmaticus. Donthwaite, Brit. M. J., II: 200 (Aug.) 1944.

Clinical Trials: Subcutaneously, 100 mgm. or more was effective in intestinal, biliary, and renal colic, flexor spasms associated with advanced sclerosis and syringomyelia, severe headache associated with intracranial tremor, sarcoma of the tibia, multiple secondary neoplasms in bone, and osteoarthritis; and ineffective in sciatica, sarcoma of diaphragm, and headache due to subarachnoid hemorrhage. Injection of 200 mgm. was followed by severe headache lasting two hours after parathesia in all four limbs which developed four hours after injection in a patient. Autopsy on a patient given 1.12 gm. showed no toxicologic changes. Injection of 100 mgm. at night induced sleep in 30 minutes, but when given during the day no soporific effect or euphoria was noted. Glazebrook and Branwood, Lancet, 249: 528; 1945.

ISOPROPENYL VINYL ETHER

(Propethylene ether)

Man—

Anesthesia: Safe induction obtained in 34 patients. Anesthetic syndrome was similar to that of ether but potency of propethylene ether was greater in man, as in animal. Induction period was shorter, and amount required was one-fourth to one-third less. Blood pressure not affected; pulse usually unaffected; respiration deep and regular; no post-operative sequels; hypoxia prevented. Davis and Krantz, Anesthesiology, 5: 159 (Mar.) 1944.

KETOSTEROIDS

Man—

Excretion. Average excretion was 14.6 mgm/liter in urine of women bearing female fetus and 26.2 mgm/liter in women bearing male fetus.

Highest value with female fetus was 19.8 mgm/liter and with male fetus was 80 mgm/liter. Burrows, MacLeod, and Warren, *Nature*, 119: 300 (Mar.) 1942.

LACTIC ACID

Aerial Disinfection: Concentrations of 10 mgm. per cubic meter of air killed 90% of bacteria in five minutes at humidities ranging from 40 to 85% and from 60 to 80% respectively Lovelock, Lidwell, and Raymond, *Nature*, 153: 20 (Jan.) 1944.

LACTOBACILLUS CASEI FACTOR

(Vitamin B₆ and Synthetic)

Bacteria—

Antianemic Factor: One microgram vitamin B₆ conjugate, isolated from yeast, was equivalent to 0.003 to 0.006 microgram vitamin B₆ in stimulating growth of *Lactobacillus casei* and *Streptococcus faecalis*. Pliffner et al., *Science*, 102: 228 (Aug.) 1945.

Man—

Anemia: Initially 600 micrograms, gradually increased to 1500 micrograms per day for four weeks increased hematocrit readings and plasma globulins. Urinary excretion of B₆ factor was lowest in those with highest plasma globulin content. Sharp, Vonder Heide, and Wolters, *J.A.M.A.*, 121: 731; 1944.

Pregnancy: Intramuscularly, 5 mgm. every two to six days for two to six injections relieved nausea and vomiting Varsas, *Bol. Soc. chilena de obst. y gynec.*, 8: 401; 1943, through *Am. J. Obst. & Gynec.*, 50: 317 (Sept.) 1945.

Sprue Therapy: Intramuscularly, 15 mgm. daily brought prompt hematologic and clinical improvement in three cases. Glossitis disappeared and rapid regeneration of lingual papillae occurred, diarrhea subsided, appetite improved, well being, gain in weight. Dorby, Jones, and Johnson, *Science*, 103: 108 (Jan.) 1946.

Granulocytes. Intravenous injection of 15–20 mgm. crystalline substance in five patients with leukopenia increased within two to four and a half hours. Berry, Spies, and Doan, *South M. J.*, 38: 590 (Sept.) 1945.

Anti-anemic Properties. Intravenous injection of 20 and 50 mgm., respectively, to two patients and intramuscularly, 20 mgm. produced reticulocyte rise. Intravenously, 20 mgm. daily to three patients for 18, 1, and 13 days caused sustained rise. Orally, 50 mgm. twice a day in

three patients and three times a day in a fourth caused rise in reticulocytes, erythrocytes, and hemoglobin. Spies et al., South. M. J., 38: 707 (Nov.) 1945.

LACTOGEN

Pigeons—

Assay Methods of international standard lactogen. 50% minimum crop gland proliferation response in 20 common pigeons (300 ± 40 gm.).

1) Subcutaneously, 0.1 mgm. of international standard required = 1 international unit.

2) Shallow intrapectoral required 1.25 international unit.

3) Intradermal (micro) unit required 1/160 international unit.

Meites, Bergman, and Turner, Endocrinology, 28: 707 (May) 1941.

LAURON

(Aurothioglycolanilide in sesame oil)

Man—

Rheumatoid Arthritis: Intramuscularly, in gradually increasing doses of 25–300 mgm. to a maximum total of 3750 mgm. reduced the sedimentation rates in 40 of 55. Robinson, Canad. M. A. J., 53: 279 (Sept.) 1945.

LEAD

Rabbits—

Lead Anemia: Test for antipernicious anemia factor in liver extract was based on rapid blood response of rabbits suffering from lead anemia to injection of liver extract. 50–100 mgm. of lead in eight to ten intravenous injections of lead acetate at two day intervals produced anemia. Lourau, Bull. Soc. Chim. biol., 25: 133; 1943.

Man—

Fume Concentration: Upper accepted limit of lead concentration was 1.5 mgm. per 10 cubic meters of air. Lea and Fluck, J. Indust. Hyg. & Toxicol., 26: 94 (Mar.) 1944.

LEAD SALTS

Rats—

Chronic Lead Poisoning: 0.5 to 12 mgm/100 gm. (average 3.5 mgm) in ration caused 20–80% mortality (average 50%) among the young of the second generation. Those surviving were stunted, attaining weights of 30–45 gm. at 28 days, anemic, fur greasy Dalldorf, Science, 102: 668 (Dec. 28) 1945

Toxicity of Lead Alloy: No toxicity with lead-tin-antimony alloy containing 63.89% Pb, on receiving 300 parts Pb/million diet, while 300 parts Pb/million in form of lead acetate showed toxicity. Salomon and Cowgill, *J. Indust. Hyg. & Toxicol.*, 26, 22 (Jan.) 1944.

Guinea Pigs—

Minimum and Maximum Lethal Doses. Oral dose which will kill at least 50 and 100% of guinea pigs within seven days after administration.

	gm/kg.		
	LD ₅₀	LD ₁₀₀	Oral
Pb(NO ₃) ₂	1.33	2.0	
PbCl ₂	1.5-2	4.0	
PbSO ₄	30-35	35	
Pb ₃ (PO ₄) ₂	?	?	No toxicity up to
PbCO ₃	4	6	40 gm/kg.
Pb ₃ O ₄	2	4	
PbS	10	>20	
Pb lactate	3	4	
Pb oleate	8	12	
Pb stearate	15	>20	

(Toxicity related to solubility in inorganic salts not among organic)
Tartler, *Arch. Hyg. Bakt.*, 125, 273 (Mar.) 1911.

Man—

Polycythemia vera. Therapy over one to five years. Lead acetate orally, in 0.3 gm. capsules, later 0.2 gm. Colloidal lead phosphate intravenously, 10 ml. (each ml. containing 3.7-3.8 mgm. Pb). Nine were relatively free of symptoms. Falconer, *Am. J. Med. Sci.*, 203, 857 (June) 1912.

LEISHMANIA TROPICA VACCINE

Man—

Leishmaniasts: Subcutaneously, 0.1-0.5 ml. doses of killed vaccine injected biweekly gave successful results. Berberian, *Arch. Dermat. & Syph.*, 52, 26 (July) 1915.

LEVULINIC ACID

Rats, Guinea Pigs, Chicks—

Nontoxic when fed at 5% in diet. Tischer, Fellers, and Doyle, *J. Am. Pharm. A. (Scient. Ed.)*, 31, 217 (July) 1912.

Man—

Tolerance. No toxicity in 3 ml. oral dosage daily for 30 times. *Ibid.*

Man—

LIPIODOL

Iodism: 15 ml. instillation caused dysphagia and dysphonia, edema of glottis and tongue, edema of face, urticarial swellings over entire body, fever, increased pulse rate and blood pressure. Treated with injection of epinephrine and sodium thiosulfate saline given intravenously. White and Bayliss, M. J. Australia, 30: 421 (Nov.) 1943.

LIPOCAIC

Rats—

Fatty Livers: Prevented by addition of 1.25–5.0% in diet. Clark, Eilert, and Dragstedt, Am. J. Physiol., 144: 620 (Sept.) 1945.

LITHIUM ANTIMONY THIOMALATE
(Anthiomaline)

Man—

Microfilaria: (*W. bancrofti*) 85–100% reduction in blood with 180 mgm. daily for seven to 28 days (total 0.9–4.59 gm.). *Vomiting* with epigastric pain after total dose of 0.78–1.89 gm. Brown, J.A.M.A., 125: 952 (Aug. 5) 1944.

Lymphogranuloma venereum: Highly effective in inguinal manifestation and caused temporary arrest or recession in ano-genital syndrome. Dose intramuscularly, 0.12–0.3 gm. in aqueous solution injected two to three times a week in courses of 2–4 gm. totaling 12 to 20 injections. *Toxic Reactions*: Arthralgia and myalgia, appearing several hours after injection and lasting from one to several days. Anemia, nausea and vomiting rarely occurred. Shaffer, Am. J. Syph., Gonorr. & Ven. Dis., 26: 489 (July) 1942.

LITOMOSOIDES CARINII ANTIGEN

Diagnosis of Loiasis and onchocerciasis—

Antigen of *Litomosoides carinii* was prepared from 1% powdered dried worms suspended in 0.5% carbolyzed physiologic saline. After two hours at 37° C. this was centrifuged to form a stock extract. Intradermal injection of 0.1 ml. of the antigen caused a diagnostic wheal. Test was positive in persons with all filariasis; clinical symptoms and histologic study aid in differential diagnosis. Culbertson, Rose, and Demarest, Am. J. Hyg., 39: 152 (Mar.) 1944.

Diagnosis of Filariasis bancrofti—

Antigen of *Litomosoides carinii* gave positive skin test in 66 of 81 men who had lived approximately one year in an area where *filariasis ban-*

crofti was endemic. Precipitation tests were positive in 58 of 77 and complement fixation tests were positive in 59 of 77. *Microfilaria* were absent from blood and hydrocele fluid of all men, but disease was suspected on basis of clinical symptoms. Culbertson, Rose, and Demarest, *Am. J. Hyg.*, 39: 156 (Mar.) 1944.

LIVER EXTRACT

Man—

Infantile Pellagra: Intramuscularly, 5 ml. twice a day slowly reduced amount of fat in liver but did not restore tissue to normal. Five of seven survived. Gillman and Gillman, *J. A.M.A.*, 129: 12; 1945.

Macrocytic Anemia: 7 ml. weekly and 9 mgm. of thiamine daily improved a pregnant woman. Degazon, *Brit. M. J.* II: 461 (Oct.) 1945. Intramuscularly, 2 ml. extract on alternate days until 12 ml. given. 13 of 15 patients showed favorable response. Sundaram, *Indian M. Gaz.*, 79: 253 (June) 1944; through *Trop. Dis. Bull.*, 42: 59 (Jan.) 1945.

Aplastic Anemia or Thrombocytopenia: Intramuscularly, 4 ml. twice weekly for a month were given. No evidence of benefit. *Brit. M. J.* II: 482 (Oct.) 1945.

Anemias: Intramuscularly, 9 ml. acted as a depot for ten weeks. 1 ml. of the concentrated 15 unit extract daily for one week, maintenance dose was 2 ml. every two weeks. Sturgis, *Clin. Med.*, 52: 291 (Sept.) 1945.

Secondary Amyloidosis: Orally, 4-8 gm. three times a day for one year or more definitely prolonged life in 12 of 16 cases. Jacobi and Grayzel, *J. Mt. Sinai Hosp.*, 12: 339, 1945.

Allergy: May be erythematous and disappears with continued injection; histamine-like, when extract is injected faster than 2 ml. per minute; relieved with 0.3-0.5 ml. epinephrine (1:1,000). Engelhardt and Derbes, *South. M. J.*, 37: 31 (Jan.) 1944. Second intramuscular 2 ml. (Anahaemin), first injection 14 months before—urticaria in woman. A man with pernicious anemia acquired sensitivity to parenteral liver extract after seven years of therapy—reaction severe with complete collapse. Both responded to epinephrine, second patient maintained in health with 20 gm. stomach extract daily. Scarlett and MacNab, *Canad. M. A. J.*, 46: 578 (June) 1942.

Desensitization: 0.05 ml. extract with 0.2 ml. adrenaline 1:1,000. Dose increased every $\frac{1}{2}$ hour until 0.4 ml. given, then intramuscular administration. When 20 ml. can be given, the time between injections is increased. *Brit. M. J.*, 1: 617 (Apr.) 1945.

Pernicious Anemia: Extracts containing 15 units per ml. recommended. Huden, *Illinois M. J.*, 79: 14, 1911.

LYSINE

Bioassay—

Use of neurospora: Neurospora strain 4545 required only lysine in addition to inorganic salts, a carbon source and biotin and the growth of the organism was a function of the available lysine. Doermann, J. Biol. Chem., 160: 95 (Sept.) 1945.

Rats—

Body Weight: 20–25 mgm. lysine hydrochloride in a diet containing zein, tryptophan and B vitamins increased or maintained weight of adult rats, weighing 300–350 gm. On lysine-free diet for 50–98 days, an average of 3.5–5.6 gm. weekly was lost. Neuberger and Webster, Biochem. J., 39: 200; 1945.

Requirement: 100 mgm. per day for optimal growth of young rats. Ibid.

Deficiency: 1.5% of their initial weight (110–140 gm.) was lost weekly on a lysine-free diet for 63–85 days, mild anemia developed with 30% less hemoglobin and 20% less red blood cells. Plasma proteins were reduced 15 to 20% and the fat and protein content of the liver fell to 9.8 and 17.2% respectively as compared to 16.7 and 20.2% respectively in lysine fed rats. Gillespie, Neuberger, and Webster, Biochem. J., 39: 203, 1945.

MAGNESIUM

Chicks—

Requirement: Minimum was 400 parts per million during first weeks of life. Almquist, Proc. Soc. Exper. Biol. & Med., 49: 544 (Apr.) 1942.

Rats—

Requirement: 50 parts per million. Ibid.

Man—

Hyperthyroid: Non-diffusible magnesium fraction was five to 58% of total serum magnesium (average $30.5 \pm 1.9\%$). In normals, fraction varied from 17 to 42% of total with an average of $30.4 \pm 1.1\%$. Bissell, Am. J. M. Sc., 210: 195 (Aug.) 1945.

Urinary Calculi: Addition of magnesium compound eliminated irritating action of "Solution G" of pH 4.0 which contained 32.3 gm. citric acid monohydrate, 3.8 gm. anhydrous magnesium oxide, 4.4 gm. anhydrous sodium carbonate and distilled water to 1000 ml. Suby, Suby, and Albright, J. Urol., 48: 549 (Nov.) 1942.

MAGNESIUM SULFATE

Birds—

Pullet Disease: 310 gm /4 liters of water for 100 birds was left with flock for 30 to 45 minutes, and then replaced with 1 ml potassium or sodium dichromate in two liters of water or 1 ml copper sulfate in eight liters of water. (Copper sulfate solution must not be given longer than four days, but dichromate can be used indefinitely.) Ryff and Stafseth, *Vet. Med.*, 37: 291 (July) 1912.

Rabbits—

Coramine Antagonism: Injection of 100 mgm and 150 mgm respectively, attenuated or completely abolished hypertensive effects due to Coramine. La Barre, *Compt. rend Soc. biol.*, 139: 66 (Jan.) 1915.

Cats—

Fatal Blood Concentration: Intravenously, 21-31 mgm /100 ml under barbiturate anesthesia, 23-50 mgm /100 ml under ether anesthesia, Moore and Wingo, *Am. J. Physiol.*, 135: 492; 1912

Cats and Dogs—

Nonfatal Concentration: 23-31 mgm /100 ml blood concentration magnesium sulfate subcutaneously in unanesthetized animal. *Ibid.*

Pain Preventive: Serum concentration of 15 mgm /100 ml with preliminary ether anesthesia was pain preventative surgical anesthesia serum concentration was 23 mgm /100 ml. *Ibid.*

Dogs—

Fatal Blood Concentration: Intravenously, 24-31 mgm /100 ml under barbiturate anesthesia, 26-54 mgm /100 ml under ether anesthesia. *Ibid.*

Gastric Motility and Secretion: 150 mgm /kg intravenously abolishes gastric hypercontractility and inhibits exaggeration of gastric secretion following insulin, but does not effect gastric hypersecretion following histamine. No curarizing properties. La Barre and Kettenmeyer, *Arch. internat. pharmacodyn. et de therap.*, 66: 305 (Sept. 30) 1911

100-150 mgm /kg. intravenously sodium barbiturate and magnesium sulfate inhibit hypersecretion of epinephrine following insulin. Due to paralysis of thalamic centers. *Ibid.* 315 (Sept. 30) 1911

Intravenously, 15 gm urea /50 ml water \pm 10 ml 2% potassium magnesium sulfate solution lowered blood pressure urea elimination retarded. Spinelli, *Quart. e. clinica*, 25: 129 (Apr.) 1911 through J. A. M. A., 117: 1655 (Nov. 8) 1911.

Man—

Angiospasm: Intravenously, in a recumbent position 10 gms of 10%

solution with glucose was given to more than 1000 patients without incident. One elderly patient with coronary sclerosis died. Pines, Brit. M. J., II: 475 (Oct.) 1915.

Convulsions: 5 ml., 25% magnesium sulfate intravenously, given slowly every other day, had sedative action, reduced number of convulsions in man with traumatic epilepsy. No ill effects, fall in blood pressure, nor diuretic action. J.A.M.A., 117: 1833 (Nov. 22) 1941.

Hypotensive Action: 10 ml. isotonic and hypertonic magnesium sulfate solution intravenously, in concentration of 7.35 and 25 per 1,000 respectively to three patients with normal blood pressures and eight with hypertension. Blood pressure lowered 10 mm. Hg in hypertensives and arteriosclerotics, 30 mm. in hypertensive and chronic or subacute nephritis, 10-15 mm. in normals. Spinelli, Cuore e circolaz., 25: 129 (Apr.) 1941; through J.A.M.A., 117: 1655 (Nov. 8) 1941.

Hyperemesis of Pregnancy: Intravenously, one to two ml. of 50% solution in ten or 20 ml. physiologic solution twice a day for ten to 15 days. Nölting and Caso, Bol. Soc. de Obst. y Genec., 20: 670; 1941; through J.A.M.A., 118: 1258; 1942.

With Mercurial Diuretics: Addition of 0.5 ml. of 20% solution prevented ventricular fibrillation in intravenous use of mercurial compounds. Pines, Sanabria, and Arriens, Brit. Heart J., 6: 197 (Oct.) 1944; through J.A.M.A., 128: 157; 1945.

Nephritic Convulsions: Slow intravenous injection of 500 ml. of 2% solution was given. Convulsions always checked by second injection. Serum magnesium concentration was high and excretion was slow. No more than 1000 ml. of 2% solution was given in 48 hours. Winkler, Smith, and Hoff, J. Clin. Investigation, 21: 207 (Mar.) 1942.

Poisoning from magnesium sulfate enema. Symptoms were heat and severe thirst. *Therapy:* 1.0 gm. calcium gluconate, intravenously (serum magnesium was 20.8 mgm/100 ml.); 0.1 gm. of calcium gluconate was given again (serum magnesium was 15.4 mgm/100 ml.). 196 mgm. of magnesium was excreted in three hours. Fawcett and Gens, J.A.M.A., 123: 1028; 1943.

Seasickness: Intramuscularly, a solution with 1.25 gm. magnesium sulfate plus 0.05 gm. caffeine, 0.25 mgm. atropine injected at twelve hour intervals for two to three injections. Poch, Dia med., 13: 798; 1941; through J.A.M.A., 118: 1258; 1942.

Serum Magnesium. Single intramuscular injection of 10 ml. of 25% solution raised average concentration of 3.8 mgm/100 ml. to 6.0 to 6.5

mgm/100 ml. in one to two hours Moore and Wingo, *Am J. Physiol.*, 135: 492; 1942.

Sphincter of Oddi Relaxed. 12 gm orally or intraduodenally. Bergh and Layne, *Am. J. Digest. Dis & Nutrition*, 9: 162 (May) 1942.

Skin Infection: Continuous wet dressing with 50% solution in glycerin was most successful for minor skin infection. In extensive superficial infection, 50% aqueous solution was used for extremities. Grindlay, *Bull. U. S. Army Med. Dept.*, # 74: 74 (Mar.) 1944.

Tetanus Spasm Control: 4 ml of 25% solution at two hour intervals for 48 hours plus phenobarbital every three hours Serum concentration was 7.0 mgm/100 ml., and 6.5 mgm/100 ml 12 hours later. Moore and Wingo, *Am. J. Physiol.*, 135: 492, 1942.

Tetany: Orally, 0.3 gm. three times a day corrected hyperirritability and low magnesium blood level (1.7 mgm/100 ml.) in six year old child. Miller, *Am. J. Dis. Child.*, 67: 117 (Feb.) 1944.

MAGNESIUM TRISILICATE

Man—

Effect. Orally, 6 gm. daily for several days increased urinary magnesium 56%, urinary pH 8%, feces pH 5.5%, and titrable urinary acidity decreased 34%. 6.5% of magnesium ingested was absorbed and excreted in urine. West and Pennoyer, *Am. J. Digest Dis*, 12: 199 (June) 1945.

MANDELIC ACID

Aerial Disinfection: 8 mgm/cu M. air was bactericidal to air-borne organisms in sprayed saliva at 70% relative humidity and 60 to 70° F. Lovelock, Lidwell, and Raymond, *Nature*, 153: 20 (Jan.) 1944.

MANGANESE

Guinea Pigs—

Storage: Various concentrations of manganese chloride were injected daily for six days and oxygen consumption values were taken. Doses between 1.0 mgm/kg. and 10.0 mgm/kg reduced amount of oxygen used. All tissues stored manganese, but thyroid stored in greater amounts than other tissues. Raynaud and Deyssach, *Proc. Soc. Exper Biol & Med.*, 51: 228 (Nov.) 1912.

Dogs—

Storage: Forty nine times normal amount of manganese was stored in thyroid with subcutaneous injection of 50 mgm manganese chloride per kilo. *Ibid.*

MANNITOL

Monkeys (Rhesus)—

Metabolism: Average liver glycogen was 0.28% after 24 hour fasting. 8 gm. mannitol/kg., given by stomach tube, showed no significant glycogen storage. 3 gm. daily fed for three months produced no histopathologic changes or toxicologic indications. Ellis and Krantz, J. Biol. Chem., 141: 147 (Oct.) 1941.

Man—

Metabolism: 10 gm. daily for one month produced no changes in non-protein nitrogen, carbon dioxide combining power of blood, or red blood cell count or kidney damage. Laxative threshold was 10 to 20 gm. Neither blood sugar level nor respiratory quotient was affected by 50 gm. Ibid.

MANNOSE

Rabbits—

Metabolism: Orally or intraperitoneally, 2 to 5 gm/kg. was well utilized with average retention of 96%. Baily and Roe, J. Biol. Chem., 152: 135 (Jan.) 1944.

MANZANILLO TREE SAP

Man—

Dermatitis: Similar to that caused by other toxic plants. *Treatment:* Cool starch or soda baths, calamine with 1% phenol, zinc ointment. Snow and Harley, Arch. Dermat. & Syph., 49: 236 (Apr.) 1944.

Keratoconjunctivitis: With temporary blindness and denudation of corneal epithelium. *Treatment:* Boric acid cool compresses, boric ointment, 0.5% tetracaine hydrochloride instillation, and irrigation with isotonic saline solution. Ibid.

Prophylaxis: Prompt immersion in sea water, preferably with eyes open for 20 to 30 minutes, followed by use of abundant soap and water. Ibid.

MAPHARSEN

(m-amino p-hydroxyphenyl arsenious oxide)

Chickens (Rhode Island Red cockerels)—

Toxicity: 0.018 gm. injected at the rate of 0.0143 gm/kg. produced severe dyspnea and weakness in five minutes, more pronounced in 15 to 25 minutes after injection. 0.024 gm. (0.0208 gm/kg.) caused death in ten to 17 hours after injection in 1120 gm. bird. Solutions stored at 40°F. for 96 hours did not show greater toxicity. McCulloch and Nicholson, Vet. Med., 36: 574 (Nov.) 1941.

Turkeys (poults)—

Therapy of Enterohepatitis Intramuscularly, 1 ml. of solution containing 0.6 gm/12 ml. boiled water. Ibid

Mice—

LD₅₀: 34 ± 0.5 mgm/kg. intraperitoneally of 0.3% aqueous solution combined with 10% aqueous solution of sodium sulfathiazole, LD₅₀ was greater with either drug alone (combined LD₅₀ was 65% of LD₅₀ of each drug.) Cranston et al., J. Pharmacol. & Exper. Therap., 81: 284 (July) 1944.

Resistance Development: In 1910, 50% of *Trypanosoma equiperdum* infected mice were cleared by 16 mgm mapharsen/kg., while in 1943 none were cleared by 40 mgm/kg Eagle and Magnuson, J. Pharmacol. & Exper. Therap., 82: 137 (Oct) 1944.

Rabbits—

Early Syphilis: Minimal curative dose was seven to 12 mgm/kg. by intravenous drip during one to four days. Eagle and Hogan, Science, 95: 360 (Apr. 3) 1942.

Dogs—

Blood Concentration 2.5 mgm/kg. was given to two dogs by one hour rapid drip method, and two received 25 mgm/kg. by syringe. Arsenic levels were, respectively, 112.5 and 375.5 microgram/100 gm. of blood immediately after administration, but were 46.5 and 43.9 microgram per 100 gm. one hour later and dropped equally later. Arsenic concentration in tissues was greater with syringe method. Gruhitz, Sultzberger, and Shaffer, Arch. Dermat. & Syph., 49: 321 (May) 1944.

Bromsulfalein Retention: Single injection of 60 mgm. caused abnormal liver function in 59% of 17 normal dogs. Dye retention occurred irrespective of dosage over a range of 27 to 91 mgm/kg. Drill and Loomis, Proc. Soc. Exper. Biol. & Med., 58: 296 (Apr.) 1945.

Cholic Acid Output consistently depressed by 60 mgm in biliary fistula dogs deprived of bile acid. A dose of 300 mgm. neoarsphenamine did not consistently depress cholic acid output. Annegers et al., Arch. Dermat. & Syph., 51: 112 (Feb.) 1945.

Toxicity: Maximum tolerated dose was 10 mgm/kg per day for five day treatment period and minimal lethal dose was 14 mgm/kg per day for the same period. Magnuson, Raulston, and Muff, Ven. Dis. Inform., 22: 431; 1941. Maximum tolerated dose by continuous intravenous drip during 12 hours each day for five consecutive days was 10 mgm/kg. per day and minimal lethal dose was 12 mgm/kg. per day. By single intra-

venous injection, maximum tolerated dose was 12 mgm/kg. and minimal lethal dose was 15 mgm/kg. Magnuson, Raulston, and Muff, Ven. Dis. Inform., 22: 157 (May) 1941.

Man—

Agranulocytosis with 0.28 gm. intravenously, in five injections within 13 days, and 0.27 gm. intravenously, in five injections within 21 days (two negro soldiers) with concomitant bismuth therapy. Kasich, Arch. Dermat. & Syph., 50: 302 (Nov.) 1944.

Ambulatory Therapy: Intravenously, 60 mgm/5 ml. water daily for 30 consecutive days was given to 107 patients. All lesions of early infectious stage healed within ten days. Goldblatt, Arch. Dermat. & Syph., 49: 403 (June) 1944.

Aplastic Anemia: 0.06 gm. twice weekly, and bismuth subsalicylate, weekly, exhibited purpura after tenth injection. Death followed. Freeman, Arch. Dermat. & Syph., 50: 320 (Nov.) 1944.

Blood Concentration: Five doses were given intravenously in one hour in five consecutive days, a total of approximately 11.78 mgm/kg. Average successive doses were: 2.83, 2.27, 2.33, 2.49, and 2.55 mgm/kg., respectively. Blood concentrations averaged 78.6 microgram/100 gm. blood immediately after first dose, 88.9 after third, and 106.2 after fifth dose. One hour after first dose, arsenic concentration fell from 78.6 to 34.4, and six and 24 hours later, 12.7 and 6.9 micrograms/100 gm. blood, respectively. Gruhitz, Sultzberger, and Shaffer, Arch. Dermat. & Syph., 49: 321 (May) 1944. Rise to 16 micrograms/100 ml. whole blood in first five days of therapy, when a total of 0.54 to 0.96 gm. was injected in six to seven days. 0.54 gm. plus typhoid vaccine for fever of 103 to 105° F. gave level of 10 micrograms/100 ml. after first day, remained unchanged on next three days, and rose to 17 micrograms/100 ml. during next three days. Siegel, Goldstein, and Goldwater, Arch. Dermat. & Syph., 46: 783 (Dec.) 1942.

Cerebral Reactions: A total of 890 to 1200 mgm. was given by slow intravenous drip in five days. Reactions in 20 of 960 cases were headache, dizziness, incoherent speech, personality changes, twitchings, convulsions, and coma. Five deaths. Convulsions were controlled by giving intramuscularly, 1 to 2 ml. of 10% B. A. L. in oil, every four to six hours. Bowman and Humphrey, Urol. & Cutan. Rev., 49: 557 (Sept.) 1945.

Fatal Cerebral Hemorrhage Intravenously, 0.03 gm. caused excruciating left-sided headache 20 hours later, followed by convulsion, coma, and death. Leider and Rogers, Am. J. Syph., Gonorr. & Ven. Dis., 28: 218 (Mar.) 1944.

Death: 0.06 gm. twice weekly for ten times (also bismuth subsalicylate once weekly) resulted in purpura. After 12 injections, characterized by faintness, temperature rise, aplastic anemia, agranulocytosis, death 19 days after initial purpura. Freeman, *Arch. Dermat. & Syph.*, 50: 320 (Nov.) 1911.

Erythema: 0.06 gm. to 12 patients and 0.01 and 0.01 gm. respectively, to two patients were administered twice weekly with bismuth subsalicylate once weekly. Continuance of therapy despite erythematous reaction six to 11 days after first dose produced severe parenchymatous damage including hepatitis, nephritis, and agranulocytosis 11 to 21 days after start of treatment. Leifer, *Am. J. M. Sc.*, 210: 158 (Oct.) 1915.

Hemorrhagic Encephalopathy: Was produced in seven of 81 patients receiving 1,200 mgm. intravenously, by slow drip method in five days. Mallery and Curtis, *J. Clin. Investigation*, 3: 95 (Nov.) 1914.

Intensive Treatment: Eight day therapy using 720 to 960 mgm. in divided doses of 0.06 gm. twice a day, combined with two episodes of five hour 103° F. artificial fever was used in 21 cases. There were two failures. Toxicity of mapharsen was increased by fever. 960 mgm. in eight days was not considered a safe dosage. Epstein, Rees and Brainerd, *Am. J. Syph., Gonorr. & Ven. Dis.*, 28: 113 (July) 1914. 1.0 mgm. kg. three times a week, injected for six to ten weeks to 61 syphilitics. 1.000 mgm. kg. was average amount required for serologic reversal. Mackee and Astrachan, *New York State J. Med.*, 11: 2577 (Dec.) 1911.

Lupus Erythematosus. Injections of 0.02 gm. biweekly (average number of injections was ten) produced good results in 21 cases. Goldberg, *Arch. Dermat. & Syph.*, 52: 89 (Aug.) 1915.

Malaria: Single intravenous dose of 0.01 gm. with 0.6 gm. quinine sulfate three times a day orally, reduced temperature to normal in a few hours in ten patients. Hospital stay of quinine resistant patient reduced from 6.5 to 3.5 days. *Recommended Dose:* four injections of 0.01 gm. each at weekly intervals. Stewart, *U. S. Naval M. Bull.*, 11: 991 (May) 1915.

Mercuric Arsenotherapy: 20 injections in doses of 0.04 gm. at daily intervals (total 1.2 gm.) were effective in early syphilis. Kolmer and Rife, *Arch. Dermat. & Syph.*, 11: 1075 (Dec.) 1911. By intravenous drip over 12 hours 240 mgm. per 2.4 liter of 5% glucose for five days was given. Total = 1.2 gm. mapharsen per patient. Careful observations and tests of 18 patients followed for more than six months. 15 had negative sero-contraction, 50 of them after one and three after two courses of therapy. Of 26 patients observed for less than six months, 17 had a negative at 1192.

positive serologic reaction. No serious toxic reactions or fatalities. Craig and Sadusk, *New England J. Med.*, 230: 314 (Mar.) 1914. (For infants and children): 4 to 6 mgm/kg. per day. First day, one-half of calculated daily dose was given; second day, three-quarters of dose; third, fourth, and fifth days, five-quarters of daily dose. Improvement noted. Levin, Hoffman, and Koransky, *Am. J. Dis. Child.*, 63: 201 (Jan.) 1942.

Myelopathy from six injections of 72, 240, 240, 250, 240, and 180 mgm. in six days, followed by recovery. Saks and Nomland, *J.A.M.A.*, 126: 560; 1914.

Prothrombin Concentration: Reduced in massive arsenotherapy (1200 mgm. each to ten patients and 50 mgm/kg. to two children). Kalz and Steeves, *Am. J. Syph., Gonorr. & Ven. Dis.*, 28: 89 (Jan.) 1944.

Sodoku (rat-bite fever): To a baby, unspecified number of intravenous injections of 2 mgm. for each injection, then 4 mgm. every five days, plus parenteral fluid and transfusions were given. Witzberger and Cohen, *Arch. Pediat.*, 61: 123 (Mar.) 1914.

Congenital and Acquired Syphilis (infants and children): Intravenous drip for five days of 3.0 to 6.0 mgm/kg. in 5% dextrose solution, 300 to 600 ml. per day for infants, and up to 1000 ml. per day for older children. Minor toxic reactions were fever, urticaria, erythema, vomiting, abdominal distention, irritability, headache, listlessness, localized phlebitis and local abscess. Levin et al., *J.A.M.A.*, 120: 1373; 1942.

Early Syphilis: Continuous intravenous drip of 0.24 gm. daily for five days. Sadusk et al., *Yale J. Biol. & Med.*, 14: 333; 1942.

240 mgm. in 2400 ml. 5% dextrose daily for five days. Usher and Hill, *Canad. M. A. J.*, 46: 342 (Apr.) 1942.

Slow intravenous drip of 240 mgm/2000 ml. 5% dextrose for five consecutive days to a total of 1200 mgm. supplemented by intramuscular injections of metallic bismuth, gave good results in 426 of 800 patients. Bowman and Humphrey, *J. Indiana M. A.*, 38: 259 (Aug.) 1945.

More than 1200 mgm. was given. A single three hour dose consisted of 60 mgm. dissolved in 500 ml. distilled water to which was added 50 ml. of 50% glucose. Repeated four times daily. Berry, *Am. J. Syph., Gonorr. & Ven. Dis.*, 26: 204; 1942.

Early and Latent Syphilis: 40 to 80 mgm. (average, 60 mgm.) three times a week for four to 12 weeks to 4,823 patients, one-third also received 0.2 gm. bismuth subsalicylate. Best results obtained when bismuth was given. Failures were 6.6, 1.5, and 1.1% respectively in those given 15 to 20, 21 to 26, or more than 26 mgm/kg. with bismuth. Eagle, *J.A.M.A.*, 126: 538; 1944.

Weil's Disease: Recovery in four of five by one or more injections of 0.6 mgm. Lorenz, U. S. Naval M. Bull., 12: 560 (Mar.) 1911.

MAPIARSIDE

(m-amino p-hydroxyphenyl arsenious oxide HC hemiacetoholate)

Man—

Syphilis: Injection of 40 mgm. daily doses given at intervals during each day, a total dose of 1,200 mgm. in five days was more effective and less toxic than neoarsphenamine. Marshall, *Nature*, 153: 187 (Feb.) 1911.

MECHOLYL

(β -acetoxy propyl) trimethyl ammonium chloride)

Man—

Effect on Electrocardiogram ("T" wave): Subcutaneously, 15 or 25 mgm. lowered all "T" waves of three leads in five subjects, developed tachycardia in all, and lowered blood pressure in four. Hartwell, et al., *J. Clin. Investigation*, 21: 109 (July) 1912.

Megacolon Therapy: 50 to 100 mgm. half hour after breakfast, increasing 50 to 100 mgm. at three to four day intervals until bowel movement or toxic symptoms resulted. Mid afternoon, 50 to 100 gm. added after seven to ten days, if necessary. Toxic symptoms were nausea, vomiting, hyperperistalsis, diarrhea, pallor, cold perspiration, cyanosis and bradycardia. Relieved promptly by 0.2 to 0.3 mgm. of atropine sulfate. Alway, *Lancet*, 62: 181; 1912.

Pancreatic Function Test: Subcutaneously 15 mgm. was given, samples of pancreatic juice were collected at 10, 20, 30, and 40 minutes with a rubber tube with two lumens passed through the pancreas into the duodenum. Bauman et al., *Am. J. M. Sc.*, 207: 281 (Mar.) 1914.

MELAMINI

Rat—

Diuretic Action: 76% times that of urea. Estimated dose was 20 mM/kg., and useful diuretic dose was 0.1 to 1.0 mM/kg. orally. Lippel and Stokes, *J. Pharmacol. & Exper. Therap.*, 84: 253 (Apr.) 1915.

Assay Results: Of 70 amides, anides, azides & urea, purine, pyrimidine derivatives, and amines derivatives, 10 were assayed tested by rat assay method of diuretic action. Melamini, a benzene & 1,1-dimethylamine were the most potent. Lippel and Hertz, *Am. J. Pharmacol. & Exper. Therap.*, 81: 54 (May) 1914.

Dogs—

Diuretic Action: 18.6 times that of urea. Maximum diuresis in one to three hours and normal reached in four to six hours after administration. Excreted as dimelamine monophosphate. Lipschitz and Stokey, J. Pharmacol. & Exper. Therap., 83: 235 (Apr.) 1945.

Man—

Diuretic Dose was 0.6 to 3.0 gm. per day. Lipschitz and Hadidian, J. Pharmacol. & Exper. Therap., 81: 84 (May) 1944.

MELANOPHORE HORMONE OF PITUITARY**Frogs—**

Bioassay: Most satisfactory test animals were hypophysectomized *Rana pipiens*. They could be used repeatedly if 24 hours elapsed between complete contraction of melanophores and re-injection. Melanophores on medial side of leg just below insertion of gastrocnemius and above smallest toe have proved constant in repose. Criterion of action was length of time required for melanophores to return to full contraction after injection (dose response in 60 to 240 minutes). Calloway, McCormack, and Singh, *Endocrinology*, 30: 423; 1942.

MELARSEN OXIDE**Man—**

Trypanosomiasis: Orally, 3 mgm/kg. for five to eight consecutive days and/or intravenously, 1 mgm/kg. daily for seven days caused fall of spinal fluid cell count in 14 of 16 patients. Parenteral route apparently gave maximum therapeutic effect, especially in neurologic involvement. Weinman and Franz, *Am. J. Trop. Med.*, 25: 343 (July) 1945.

ANTI-MELITENSIS SERUM**Man—**

Brucellosis: 50 ml. serum and 2 gm. sulfadiazine daily for two days were given, followed by 0.65 gm. daily for 11 days in a case of brucellosis following cystostomy. Ewell, *Urol. & Cutan. Rev.*, 49: 544 (Sept.) 1945.

MENADIONE

(2-methyl-1,4-naphthoquinone)

Chicks—

Toxicity LD₅₀ was orally, 804 mgm/kg. \pm 0.81%; non-lethal dose was 750 mgm/kg. Ansbacher, Corwin, and Thomas, J. Pharmacol. & Exper. Therap., 75: 111 (June) 1942.

Mice—

Acute Toxicity: LD₅₀ was 620 mgm/kg. orally, and 138 mgm/kg. subcutaneously. Ibid.

Local Irritation: Subcutaneously, 0.5 mgm showed no irritation. Ibid.

Rabbits—

Lethal Dose: 230 to 280 mgm/kg. as single oral dose. Ibid.

Chronic Toxicity: 28 to 36 daily oral doses of 4 mgm/kg. were well tolerated; seven subcutaneous injections of 20 mgm/kg. did not cause anemia or pathologic changes in vital organs, but did produce marked local irritation and sloughing. Ibid.

Hyperprothrombinemia after single oral dose of 5 mgm/kg. Field and Link, J. Biol. Chem., 156: 739 (Dec.) 1944.

Cats—

Chronic Toxicity: 72 repeated oral doses of 2 mgm/kg. or 13 oral doses of 50 mgm/kg. produced no toxic effects. Five to seven subcutaneous injections of 20 to 25 mgm/kg. produced a marked anemia and local sloughing, but no lesions elsewhere. Seven subcutaneous injections of 20 mgm/kg. constituted a lethal dose. Ibid.

Hyperprothrombinemia after single oral dose of 20 mgm/kg. Field and Link, J. Biol. Chem., 156: 739 (Dec.) 1944.

Dogs—

Hyperprothrombinemia after single oral dose of 10 mgm/kg. Ibid.

Local Irritation: Intramuscularly, into the long head of triceps 2 and 4 mgm. in oil caused slight and moderate degeneration, 6 mgm. in oil injected into vastus lateralis resulted in necrosis. Ansbacher, Corwin, and Thomas, J. Pharmacol. & Exper. Therap., 75: 111 (June) 1912.

Chronic Toxicity: Repeated oral doses of 2 mgm/kg. produced no injurious effects; repeated oral doses of 25 to 50 mgm/kg. did not result in permanent injury, but produced a severe temporary anemia in one animal receiving a total of 23 gm. Seven subcutaneous injections of 20 mgm/kg. produced definite anemia and sloughing wounds, one of two animals died but no pathologic lesions were observed. Repeated injections of 50 mgm/kg. resulted in anemia and hemoglobinuria, this dose was fatal for one animal after four injections. A single subcutaneous injection of 90 mgm/kg. produced a transitory increase in hemoglobin and in red blood cells followed by marked anemia. Ibid.

Intravenous Toxicity: Three injections of 5 mgm/kg. given over a

period of three to seven days, caused a slight temporary anemia, but no other toxic signs. No pathologic lesions were observed. *Ibid.*

Monkeys—

Chronic Toxicity: 1 mgm/kg., given in repeated oral doses, caused no toxicity, anemia, or pathologic lesions. *Ibid.*

Local Irritation: Subcutaneously, 0.5 mgm. in oil produced no local irritation; subcutaneously, 1 to 2 mgm/kg. in oil caused slight induration and local development of small nodules. *Ibid.*

Man—

Hemorrhage in Newborn: Prevented with 2.0 mgm. orally, three times a day, three to six weeks prior to labor or 10 to 20 mgm. during labor. Treatment with 2 mgm. in oil, intramuscularly. Pray, *Lancet*, 61: 1; 1944.

Hepatitis (hemorrhagic): Hemorrhage was controlled by blood transfusion from donors who received 3.2 to 30 mgm. menadione orally, intramuscularly, or intravenously, or vitamin K from fish meal six to 48 hours before transfusion. Kinsey, *Arch. Int. Med.*, 73: 131 (Feb.) 1944.

Hypertension: Parenterally, 1 ml. was given every six hours for coronary thrombosis. Prothrombin values were 40 to 70% of normal in six to 12 hours after initial attack. Therapy continued until level reached 90%, then drug continued orally to maintain level above 85% of normal. Doles, *South. M. J.*, 35: 461 (May) 1942.

Liver Function Test: In 86 patients the level of plasma prothrombin (if below 80%) was index of liver performance while absence or presence of response to intramuscular 2 mgm. indicated whether any depression of this function respectively was or was not due to organic liver function. This was useful in differentiating between jaundice of intrahepatic and extrahepatic origin. Andrus, Lord, and Lake, *Ann. Surg.*, 115: 1015 (June) 1942.

Infant Mortality: 3.2 mgm. parenterally to mothers just prior to delivery resulted in death rate of 29.8 in 1000 births and 25.8 in 1000 births in controls. Potter, *Am. J. Obst. & Gynec.*, 50: 235 (Sept.) 1945.

Abnormal Prothrombin Time in tuberculous was restored by administration of 3.2 mgm. daily. Farber and Miller, *Am. Rev. Tuberc.*, 48: 406 (Dec.) 1943.

Vitamin K Deficiency due to impaired absorption of food fat improved with 2 to 3 mgm. per day orally. After saturation occurred, 1 mgm. per day was adequate. McIntosh, *Bull. New York Acad. Med.*, 20: 25 (Jan.) 1944.

MENINGOCOCCAL ENDOTOXIN

Rabbits—

Penicillin Effect. Endotoxin intravenously and subcutaneously 10,000 to 20,000 units of penicillin every few hours saved 11 of 16 animals, all controls died. Boor and Miller, *Science*, 102: 427, 1945

MENINGOCOCCUS ANTISERUM

Man—

Waterhouse-Friderichsen Syndrome. One patient received 80,000 units intravenously, plus desoxycorticosterone intramuscularly in the first 18 hours of therapy and sulfadiazine sodium in doses sufficient to maintain blood levels of 15 to 20 mgm/100 ml. Another patient received sodium sulfadiazine, antiserum, oral sulfadiazine and 50 ml adrenal cortical hormone, given intravenously, daily. Death from hepatorenal failure. Marangoni and D'Agati, *Am. J. Med. Sci.*, 207: 385 (Mar.) 1944

MERCUPURIN

(Na N-[β -methoxy- α -(9-thiophylline mercury) propyl] 1,2,2-trimethylcyclopentene 1,3-dicarboxylate acid monamide)

Cats—

Fatal Dose: 0.83 ml/kg., intravenously (1 ml. = 10 mgm. Hg); deGraff and Lehman, *J.A.M.A.*, 119: 998, 1944

Man—

Fatalities: Immediate deaths resulted in three given slow intravenous injection of 2 ml. All had received the drug previously. Friedfeld et al. *J.A.M.A.*, 117: 1806, 1944.

Optimal Dose. Intramuscularly, 1 ml. twice weekly was better in ambulatory patient with congestive heart failure. Diuretic effect was determined by weighing patient in evening immediately before an injection and also 12 to 15 hours later. Modell *Ann. Int. Med.*, 20: 265 (Feb.) 1944.

MERCURIC CHLORIDE

In Vitro—

Germinol Activity. 1:12,500 dilution killed *Vibrio cholerae* aureus with addition of 2% concentration of glucose, maltose or sucrose. In presence of (M:15) equimolar concentrations of solutions of glycine, aspartic acid, glutamic acid, arginine and lysine, highest dilution fell to 1:2,500. Salle and Ginnora, *Proc. Soc. Exper. Biol. & Med.*, 54: 85 (Oct.) 1944

Chick Embryos—

Lethal Dose: Smallest amount causing death was 0.002 gm/kg. Dunham, Proc. Soc. Exper. Biol. & Med., 50: 274 (June) 1942.

Turkeys—

Hexamita Meleagridis: 1:8,000 solution as drinking water had no therapeutic effect, but was nontoxic. 1:2000 solution was fatal to four of five poults and 1:4000 dilution caused definite stunting and a tendency to perosis. McNeil and Hinshaw, Poultry Sci., 24: 516 (Nov.) 1945.

Dogs—

Hypoproteinemia had protective effect against intravenous injection of mercuric chloride, 3 mgm/kg. which killed other dogs. Holman and Bonnelly, J. Exper. Med., 76: 511 (Dec.) 1942.

Man—

Lethal Dose: Smallest amount causing death was 0.001 to 0.002 gm/kg. Dunham, Proc. Soc. Exper. Biol. & Med., 50: 274 (June) 1942.

Pityriasis rosea Therapy: 1:15,000 dilution baths twice daily for ten minutes at a time for one to two weeks. Skin became dry, crackly, and scaly and disease was controlled. There was no toxic absorption. Sutton, South. M. J., 35: 597 (June) 1942.

MERCURIN

Cats—

Fatal: 0.70 ml/kg. intravenously (1 ml. = 40 mgm. Hg). deGraff and Lehman, J.A.M.A., 119: 998; 1944.

MERCURY

Cats—

Fatal Dose was 15 mgm/kg. when administered as mercuric chloride, or mercuric chloride with theophylline, or salyrgan (mersaly). However, mercury administered as salyrgan-theophylline, mercurin, or mercupurin (mercurophylline) was half as toxic, the fatal dose being 30 mgm/kg. Modell and Krop, Proc. Soc. Exper. Biol. & Med., 55: 80 (Jan.) 1944.

Man—

Water Soluble Mercury. 10 or 20% aqueous dispersion of mercury made by combining a mixture of 70 gm. cetyl alcohol and 30 gm. mercury with sodium lauryl sulfate, diacetyl sulfo succinate, glycerin, and water. 4 gm. urethral instillation, twice a day for three days caused no irritation. Maren and Edwards, J. Am. Pharm. A. (Scient. Ed.), 32: 255 (Oct.) 1943.

MERCURY CYANIDE**Dogs—**

Dirofilaria immitis. 22 injections of 0.34 mgm mercury per kg. caused poisoning, but without beneficial results. Four daily injections of 1.0 mgm mercury per kg. caused death without apparent reduction in number of microfilariae or injury to adult parasites. Lawton et al., Am. J. Trop. Med., 25: 263 (May) 1945.

MERCURY OXYCYANIDE**Dogs—**

Dirofilaria immitis: 24 injections of 1.0 mgm/kg. of mercury caused poisoning but no change in microfilarial counts. Lawton et al., Am. J. Trop. Med., 25: 263 (May) 1945.

MERCURY SUCCINIMIDE**Dogs—**

Dirofilaria immitis: 11 injections of 0.7 mgm/kg. of mercury caused poisoning, but no changes in microfilarial counts. Lawton et al., Am. J. Trop. Med., 25: 263 (May) 1945.

MERPHENYL NITRATE

(Basic phenyl mercuric nitrate)

Rabbits—

M.L.D.: Intravenously, 7 ml. of an 0.067% (1:1500) aqueous solution of basic salt buffered with 0.1% boric acid. Orally, was approximately three times the intravenous dose. N. N. R., J. A. M. A., 117: 1784; 1941.

MERSALYL**Cats—**

Fatal Dose: 0.41 ml/kg. and 1.11 ml/kg. with theophylline (1 ml. = 40 mgm. Hg). deGraff and Lehman, J. A. M. A., 119: 998, 1944.

Man—

Congestive Heart Failure. Intravenously, 2 ml., repeated three days later. Patient voided 3000 ml. of urine after each injection. Boharas and Cripp, Ann Int Med., 23: 426 (Sept.) 1915.

Intravenous solution of mersalyl theophylline containing 0.1 gm. mersalyl and 0.05 gm. theophylline per ml. was compared with oral, enteric coated tablets containing 0.08 gm. mersalyl and 0.04 gm. theophylline, five tablets as single dose in morning. Intravenous route had greater

diuretic effect as measured by urine output and weight-loss. Toxic reactions from oral administrations only, which were loose stools, emesis, and epigastric burning. Carryer and Smith, *M. Clin. North America*, 28: 911 (July) 1944.

Treated with 400 mgm. mersalyl plus 200 mgm. theophylline for three doses at four to six day intervals. Digitalized patients received, additionally, ammonium chloride 3 gm. daily. Weight loss was 2.7 to 10.4 kg., urinary output increased 400 to 600 ml. Contraindicated in acute nephritis, colitis, and melena, chronic renal disease, a low or fixed specific gravity urine, and nitrogen retention in blood. Dickens, *New Orleans M. & S. J.*, 94: 344 (Jan.) 1942.

Vitamin C: Effectiveness of drug was enhanced by salts producing acidosis. When ammonium salts had no effect, 500 mgm. cevitamic acid was used. Shubin, *Manitoba M. A. Rev.*, 25: 50 (Feb.) 1945.

MERTHIOLATE

(Sodium ethyl-mercuri-thiosalicylate)

Spinal Fluid—

Bacteriostatic: 0.1 ml., 1% for transportation of spinal fluid specimens, in test tubes. Concentrations of 1:1000 and 1:10,000 did not alter test findings. Harris and Maloney, *Ven. Dis. Inform.*, 25: 46 (Feb.) 1944.

METAPHEN

(5-hydroxymercuri-4-nitro-o-cresol-anhydride)

Rabbits—

Reaction of Vascular Connective Tissues of ears in moat chamber. 1:10,000 dilution caused no appreciable injury; 1:8000, 1:5000, and 1:2500 caused no serious injury in 12 hours; 2:2500 caused injury when in contact for more than 12 hours, and four days continuous contact destroyed blood vessels. 1:1500 produced this effect within 22 hours 70% alcohol produced extensive hemorrhage in 15 minutes. Abell, *Anat. Rec.*, 81: 477 (Dec.) 1941.

Man—

Vincent's Infection: Gums and interproximal spaces were saturated with 1:200 tincture metaphen or 10% sodium carbonate. Mouth was irrigated three or four minutes, three or four times a day with an arsenical preparation and tincture of metaphen applied again. Neuman, *J. Canad. Dent. A.*, 10: 13 (Jan.) 1944.

Vincent's Ulceration: 1:500 solution cured three and improved five of 13 Stammers, *Proc Roy. Soc Med.*, 37: 567 (Aug.) 1944.

METHENAMINE

Quantitative Determination—

Chemical Assay: In presence of sodium bicarbonate and bromide, ammonia was oxidized quantitatively to nitrogen and water by calcium hypochlorite. Assay was based on this reaction after conversion to ammonium sulfate. Slowick and Kelley, *J. Am. Pharm. A. (Scient. Ed.)*, 51: 15; 1912.

METHERGIN

N-(α -[hydroxymethyl] propyl)-d lysergamide)

Man—

Postpartum Hemorrhage: Intravenously, 0.2 mgm. in 1 ml. solution immediately following birth of child but before delivery of placenta, caused blood loss of 113.21 ml. Loss was 168.07 ml. when drug was given intramuscularly. Tritsch and Schneider, *Am. J. Obst. & Gynec.*, 50: 431 (Oct.) 1915.

Oxytocic: Intravenously, 1 ml. caused less than 100 ml. blood loss in 91% of 271 women in labor. Uterus contracted within 20 to 30 seconds after injection and continued to act for six to eight hours. Patients also received one tablet (0.25 mgm. active ingredient) three times a day for two days. Brougher, *West. J. Surg.* 53: 276 (Aug.) 1915.

METHIONINE

Chicks—

Growth Factor: 1% d,l methionine required in diet was replaceable by combination of d,l homocystine and choline but not by cystine, homocystine or creatine alone. Klose and Minquist, *J. Biol. Chem.*, 139: 167 (Apr.) 1911.

Rats—

Experimental Burns: 1% synth. in d,l methionine was beneficial in reducing urinary nitrogen. Croft and Peters, *Lancet*, 1: 295 (Mar.) 1915.

Fatty Livers: Prevented by addition of 0.5% in diet. Clark, Lilient, and Dragstedt, *Am. J. Physiol.* 141: 620 (Sept.) 1915.

Dogs—

Protective Action against liver injury from napharsen: Orally, 2 to 4 gm., 20 to 24 hours prior to napharsen was protective and dogs tolerated 0.015 gm./kg. without uterus development. Normal dogs tolerated 0.005 to 0.005 gm./kg. of napharsen whereas in protein depleted dogs 0.002 to 0.0025 gm./kg. caused liver injury with jaundice. Goodell, Hannon, and Hawkins, *J. Exper. Med.*, 79: 625 (Jun.) 1914.

Man—

Arsphenamine Jaundice: 2.5 to 5 gm. daily for seven days. Serum bilirubin fell to normal in 19.7 days in 33 patients. Exacerbation of symptoms occurred in 12% and relapse in 3%. Peters et al., Quart. J. Med., 14: 35 (Jan.) 1945.

Burn Therapy: 5 gm. daily administration was suggested for burn patients too weak to eat well. Croft and Peters, Nature, 155: 175 (Feb.) 1945.

Infectious Hepatitis: 5 gm. daily had no effect in 18 patients. Higgins et al., Brit. M. J., I: 401 (Mar.) 1945.

50 gm. daily to 50 patients. Wilson, Brit. M. J., I: 399 (Mar.) 1945.

2.5 gm. twice daily of d,l-methionine had slightly beneficial but statistically insignificant effect. Wilson, Pollock, and Harris, Brit. M. J., I: 399 (Mar.) 1945.

Intravenously, 10 gm. daily produced dramatic results in two cases. Barclay, Kenney, and Cooke, Brit. M. J., II: 298 (Sept.) 1945.

Toxic Hepatitis Therapy: Orally, 3 to 8 gm. daily for four days to seven weeks (average 13 days) caused no death among 30 patients. By duodenal tube, 8 gm. per day markedly improved two patients after 48 hours. Am. J. M. Sc., 210: 374 (Sept.) 1945.

**N-(p-METHOXYPHENYL)-N-DIMETHYLAMINOETHYL
α-AMINOPYRIDINE
(2786 R.P.)**

Guinea Pigs—

Antihistamine Action: Subcutaneously, 1 mgm. tolerated 75 times M.L.D. histamine (0.6 mgm/kg.). Sensitivity to histamine given intravenously decreased 2, 30, and 100 times respectively followed intravenous injection of 1, 5, and 10 micrograms. Concentrations of 10^{-7} and 10^{-8} relieved violent contractions of guinea pig intestine due to histamine concentration of 10^{-7} . Bovet and Horclois, Comp. rend. Soc. de biol., 138: 99 (Feb.) 1944.

**2-METHYLAMINOHEPTANE
(Oenethyl)**

Man—

Vasopressor Action: Intramuscularly, 75 to 100 mgm. was effective dose to prevent hypotension or to restore a fallen blood pressure. Intravenously, therapeutic dose varied from 10 to 50 mgm. (average 15 mgm.) and was most effective in divided doses of 10 mgm. at half minute intervals.

Prolonged Feeding: 80 rats given 182 mgm. daily for eight months in food and water showed normal food intake, weight gain and no gross or microscopic tissue changes. Deichman and Witherup, J. Lab. & Clin. Med., 28: 1725 (Nov.) 1943.

Rabbits—

Conjunctival instillation of 1% solution two or three times a day for three months did not cause ocular tissue injury. Swan, Arch. Ophth., 33: 378 (May) 1945.

Dogs—

Plasma Substitute: Intravenously, 120–130 ml. solution was prepared by dissolving 2 gm. methyl cellulose in 100 ml. saline. This stock solution was diluted to 0.25–1% by addition of a solution containing 2 gm. ascorbic acid, 1 gm. calcium glucuronate, 1 gm. glycine, 0.5 gm. cysteine hydrochloride. Hueper, Martin, and Thompson, Am. J. Surg., 56: 629 (June) 1942.

Man—

Colloid Laxative: 10 gm. per day dose approximately doubled volume of stool and increased frequency in three normals. Each gm. increased stool approximately 10 gm. No colicky or griping pains. Tainter, Proc. Soc. Exper. Biol. & Med., 54: 77 (Oct.) 1943.

Ophthalmology: 3% sulfamerazine in 2% aqueous methyl cellulose solution produced average concentration of 42 mgm/100 gm. tissue from lower fornix and 18 mgm/100 gm. from extreme upper fornix one-half hour after instillation in normal conjunctiva; 0.5–1% of methyl cellulose in 0.9–1.2% sodium chloride was satisfactory with contact lenses; 0.5% was effective substitute for natural secretion. Swan, Arch. Ophth., 33: 378 (May) 1945.

METHYLDIHYDROMORPHINONE

(Metopon)

Man—

Analgesic: 5 mgm. was minimal effective clinical dose. Advantages over morphine (10 mgm.) were less rapid development of tolerance and dependence, rapid diminution or disappearance of tolerance during abstinence, few side effects, less hypnosis in relation to analgesia.

Disadvantages: Dangerous respiratory depression in inhalation anesthesia; therefore, morphine was most reliable. Lee, J. Pharmacol. & Exper. Therap., 75: 161 (June) 1942.

METHYLENE BLUE

Man--

High Altitude: Orally, 0.2-0.4 gm., 20 minutes to four hours before exposure increased oxygen levels 6-19% and maintained normal performance rates for one to three days, plus breathing additional oxygen at 18,000 to 48,000 feet 0.6 gm given 1½ hours before exposure to 16,000 to 20,000 feet altitude pressures without additional oxygen produced 88-90% performance. Brooks, J. Aviation Med, 16: 250 (Aug.) 1945.

P-METHYL SULFONYL-BENZAMIDINE HYDROCHLORIDE

(V187)

Mice--

Tetanus: Intramuscularly, a single dose of 10 mgm of 5% aqueous solution, given two hours after infection with *Clostridium tetani*, was 100% effective. Orally, 2.5 gm/kg. was tolerated. Evans, Fuller, and Walker, Lancet, 219 336 (Sept) 1915.

Guinea Pigs--

Tetanus: 100 mgm/500 gm in 10% solution, given two hours after infection with *C. tetani* gave effective protection. Orally, 0.1 gm/kg. was lethal within four to five days. Oral doses of 0.02 gm/kg. were sometimes fatal, but intramuscularly, five doses of 9.2 gm/kg in 24 hours were tolerated. Ibid.

Rabbits--

Toxicity. Orally, 0.5 gm/kg was tolerated, but a 1 gm dose caused toxic reactions. Ibid.

γ -METHYLTHIOPSEUDOUREA SULFATE**Man—**

Circulatory Effects: Two doses of 0.4 gm. at 30 minute intervals decreased heart rate 20 beats a minute to below 50. Orally, 0.2 to 0.4 gm. slowed heart and raised blood pressure; intravenously, 0.2 to 0.4 gm. promptly raised blood pressure which was sustained for 15 to 60 minutes in 20 moribund patients. Smirk, Brit. M. J., II: 510 (Oct.) 1941.

METRAZOLE

(Pentamethylenetetrazole)

Rats—

Subconvulsive Dose: 3 mgm. Chauchard et al, Compt. rend. Soc. de biol., 217: 619; 1943.

Guinea Pigs—

Subconvulsive Dose: 3 mgm. Ibid.

Effect: 75 mgm/kg. (5% solution) intraperitoneally, produced alternate tonic and clonic convulsions in 100% and deaths in 85%. Partial protection by sodium, potassium, or calcium salts (150 mgm/kg. in 10% solution) intraperitoneally, prior to metrazole. Wastl, Am. J. Physiol., 133: 483 (June) 1941.

Rabbits—

Cortical Depression: Higher centers depressed and lower excited, when studied with subconvulsive doses of 3 to 15 mgm. Chauchard et al., Compt. rend. Soc. de biol., 217: 619; 1943.

Pentothal Antagonist: Animals anesthetized with 25 mgm/kg. of pentothal sodium as 2.5% solution, recovered completely within ten minutes after intravenous injection of 100 mgm/kg. of metrazole, and 19 to 53 minutes without antagonist. Average recovery from 55 mgm. pentothal, intravenously or intraperitoneally, shortened from 48 minutes to five minutes with 50 mgm/kg. of metrazole. Pickrell and Richards, Ann Surg., 121: 495 (Apr.) 1945.

Cats—

Anesthesia: Subcutaneously, 0.25 ml. to support depressed respiration and circulation, was followed by intravenous injection of 1 ml. nembutal and 5 ml. 25% glucose perfusion solution. If profound respiratory depression resulted or blood pressure fell to shock levels during surgery, 0.25 to 0.5 ml. metrazole was injected intravenously or subcutaneously. At conclusion of operation, 0.5 ml. of 10% metrazole was given routinely followed in half hour by 0.5 ml. intramuscularly. Additional doses were given as further stimulation was needed. Pleuger, J. Am. Vet. Med. A., 101: 89 (July) 1942.

Dogs—

Analeptic: 0.05 ml/kg. of 10% solution (dose equivalent of 3.5 ml. for man) injected intravenously as soon as animal passed into deep surgical anesthesia, but before appearance of respiratory arrest. There were no failures when artificial respiration and oxygen were also administered in treatment of 25, 30, and 37 respiratory arrests produced by ether, divinyl ether, and chloroform, respectively. Whitehead and Draper, Surg., Gynec. & Obst., 74: 1020, 1942.

Pentothal Antagonist: Profound sleep not interrupted, but with 40 mgm/kg. of sodium pentothal, recovery time was cut by 20 to 27 mgm/kg metrazole, intravenously at first sign of awakening. Pickrell and Richards, Ann. Surg., 121: 495 (Apr.) 1945.

Man—

Barbiturate Poisoning: Patient responded promptly to 5 ml intravenously, followed by 2 ml. every two hours. 25, 0.1 gm Delvinal sodium had been taken. Walker and Teague, Virginia M Monthly, 69: 92 (Feb.) 1942.

Convulsive Therapy: To insure grand mal seizure with every dose administered, initial dose suggested was 8 to 11 ml. intravenously, with subsequent increase of 0.1 ml. for each second of latent period in excess of three to five seconds. Ziskind and Ziskind, J. Nerv. & Ment. Dis., 99: 889 (June) 1944.

Pentothal Antagonist: 5 ml. intravenously, immediately after operation under pentothal sodium, revived immediately or within 45 minutes all but 16 of 300 patients. Pickrell and Richards, *Ann. Surg.*, 121: 495 (Apr.) 1945.

Schizophrenia: Combined therapy with insulin in 100 patients with 7% vertebral fractures (43% metrazol alone). Four and one-half hours after insulin hyperglycemia, 10% metrazole was given intravenously, average effective dose being 6.6 ml. Insulin injections averaged 50 and metrazole 20 per patient. Notkin et al., *J. Nerv. & Ment. Dis.*, 97: 63 (Jan) 1943.

METYCAINE

(3(2-methyl-1-piperidyl)-propyl benzoate hydrochloride)

Man—

Caudal Block: Obtained in 72 of 77 patients with 1.0 or 1.5% solution. Volpitto et al., *South. M. J.*, 37: 83 (Feb.) 1944.

Continuous Caudal Anesthesia: Initial dose of 30 ml. of 1.5% metycaine caused saddle anesthesia in five minutes, analgesia of scrotal and vulval area within ten minutes, and to the tenth thoracic segment at end of 30 minutes. Blood pressure effects were minimal. Southworth and Hingson, *Ann. Surg.*, 118: 945 (Dec.) 1943.

Injection of 20 or 30 ml. of 1.5% solution was effective for 30 to 45 minutes. McClellan and Williams, *Am. J. Obst. & Gynec.*, 48: 617 (Nov.) 1944.

In Obstetrics: Three injections for a total of 30 ml. 1.5% caused pain perception to disappear, but uterine contractions continued with pre-anesthetic intensity and frequency in 232 and failed in seven. Average first stage of labor in multipara lasted 1.75 hours and 3.5 hours in primipara. Levine et al., *Am. J. Surg.*, 64: 31 (Apr.) 1944.

MINERAL OIL

Man—

Laxative: Rectally, 10 to 30 ml. at bedtime was effective in alleviating severe to mild cases of rectal irritation or constipation in 200 patients. Small doses after each evacuation used for hemorrhoids. For babies and children and those unable to retain at least 10 ml. of oil, petroleum jelly was used. Atonic constipation was treated with 25 gm. of 2:1 mixture of petroleum jelly and mineral oil, rectally, after morning evacuation, and 25 to 50 gm. at bedtime. Anderson, Carrington, and Brooks, *North Carolina M. J.*, 5: 87 (Mar.) 1944.

MONOCAINE FORMATE

(2-isobutyl-aminocethyl p-aminobenzoate formate)

Rabbits—

Minimal Lethal Concentration (intraspinal) was 12% in unpremedicated animals. Co Tin et al., J Pharmacol & Exper. Therap., 75: 157 (June) 1912.

Cats—

Minimal Lethal Concentration (intraspinal) was 25% in animals premedicated with pentobarbital sodium. Ibid.

Minimum Anesthetic Concentration was 0.5% Ibid.

Man—

Caudal Anesthesia 30 ml. of 1.0 or 1.5% was given initially, then 10 ml. as needed. Maximum amounts given were 1.05 gm. in 1.5% solution during labor of four hours and 1.6 gm. in 1% solution in labor lasting 3.25 hours. Roventine and Uppgar, Anesthesiology, 5: 10 (Jan) 1911.

MONACRIN

(5-aminocridine hydrochloride)

Man—

Wound Therapy Local application of gauze swabs soaked in 1:1000 solution in 0.45% saline. 1:1000 solution infiltrated into floor and margin of wounds, and 1 to 30 ml. solution injected, depending on size of wound. Arden, M. J. Australia, 32: 186 (May) 1915.

MONOCHLORACETIC ACID

Rabbits—

Reaction: None when 5% solution was applied to skin or 1% was instilled in eyes. Morrison and Lake, Univ. of Calif. Publ. in Pharmacol., 1: 397; 1911.

Man—

Effect. None with 300 ml. of 0.05% solution taken daily for 60 days. Ibid.

MORPHINE

Mice—

Analgesia (with amphetamine) Analgesic effect obtained with 20.0 mgm. morphine sulfate plus 55 mgm. alpha amphetamine per kg. was greater than greatest analgesic effect obtained with 20.0 mgm. morphine sulfate per kg. alone. With former dose analgesic effect was 40% greater, lasted longer, animal did not sleep and there was no Straub reaction. Coetzl, Buttrill, and Ivy, Proc. Soc. Exper. Biol. & Med. 55: 218 (Apr) 1944.

Rats—

Cortical Activity: Less than 20 mgm/kg. had no effect on cortical electrical activity; 20 to 50 mgm/kg. increased in amplitude and decreased in frequency; 200 mgm/kg. or 40 to 100 mgm/kg. with 9 to 30 mgm/kg. of barbiturate decreased amplitude and finally abolished cortical electrical activity. Cahen and Winkler, *Yale J. Biol. & Med.*, 16: 239 (Jan.) 1914.

Hamsters—

Dosage Levels: Sex, age, weight, and mode of injection had no apparent effect on response to morphine sulfate. Doses up to and including 150 mgm/kg. had no effect; 300 mgm. caused salivation, increased activity, hyperirritability; 500 to 600 mgm. levels caused discomfort, tonic non-fatal convulsions, analgesia, perspiration, excessive salivation, and defecation. There were no fatalities until LD₅₀ of 1250 mgm/kg. was reached; LD₁₀₀ was 1750 mgm/kg. Houchin, *Proc. Soc. Exper. Biol. & Med.*, 54: 339 (Dec.) 1943.

Rabbits—

Depressant Effects upon respiration for seven derivatives in which phenolic OH group at C-3 had been blocked were studied. 2,4 dinitrophenylmorphine was stronger than morphine in small doses though weaker in doses larger than 0.3 mgm. Sumwalt, Wright, and Miller, *J. Pharmacol. & Exper. Therap.*, 73: 246 (Nov.) 1941.

Effect on Labor: 13 mgm/kg. intravenously, at time of onset of labor caused analgesia of maternal animals but no loss of consciousness. Eight litters of 45 fetuses were all born alive by hysterectomy at 12 minutes to 15 hours interval. For 12 to 20 minutes, marked fetal narcosis was noted and in 12 to 15 hours crawled actively. There were 70% stillbirths in spontaneous births. Snyder and Lim, *Proc. Soc. Exper. Biol. & Med.*, 48: 199 (Oct.) 1941.

Cats—

Central Nervous System Effect: 2 to 5 mgm/kg. caused disintegration of adaptive behavior; 10 to 15 mgm/kg. brought on delayed stimulant action such as startle response and spontaneous running. Wikler, *J. Pharmacol. & Exper. Therap.*, 80: 176 (Feb.) 1944.

Dogs—

Prolonged Anesthesia: Subcutaneously, 2.0 to 4.4 mgm/kg. of 2% solution caused decline in rectal temperature from 38.5°C. to 34 to 37°C., followed in one to three hours by a sharp reduction in cutaneous blood flow. Green et al., *Am. J. Physiol.*, 140: 177 (Nov.) 1943.

Antidiuretic Action: Water, administered 40 ml/kg. orally, or 25

ml/kg. by intravenous infusion, was excreted quantitatively in three hours. Water by stomach was completely absorbed from gastro-enteric tract in 40 minutes. Morphine, administered 40 minutes after administration of water by stomach or 15 minutes before intravenous infusion, inhibited diuresis. Excreted amount was two to 15%. de Bodo, J. Pharmacol. & Exper. Therap., 82: 74 (Sept.) 1944.

Man—

Blood Flow: Rate of blood flow increased with morphine injection. Greater effect was obtained with 10 and 20 mgm. than with 40 and 60 mgm. in normal subjects, drug addicts, or post-addicts. Himmelsback, J. Pharmacol. & Exper. Therap., 80: 343 (Apr.) 1944.

Colon Effect: 8 to 16 mgm. intramuscularly, increased tone and amplitude of non-propulsive type of rhythmic contractions, and decreased propulsive activity of ileum and colon segments, respectively. Adler, Atkinson, and Ivy, Arch. Int. Med., 69: 974 (June) 1942.

Pain Perception: Threshold of perception of cutaneous pain increased from 0 to 56% (average 20%) in 24 subjects one and a half hours after injection of 0.24 mgm/kg of morphine sulfate, average increase was 19%, one and a half hours after subcutaneous injection of 0.06 mgm. monoacetylmorphine hydrochloride per kilo Jones et al., Arch. Int. Med., 73: 322 (Apr.) 1944.

Respiratory Effect: 10 to 15 mgm. morphine sulfate decreased minute volume of respiration an average of 13.6% within three to seven minutes and 13.1 and 11.6% during 16 to 20 and 31 to 35 minute post-injection period, respectively. Intramuscularly, 10 to 20 mgm. morphine sulfate depressed minute volume 2.7% during three to seven minute post-injection period. Intravenously or intramuscularly, 10 mgm. caused Cheyne-Stokes respiration in five of 15 of those over 68 years. Dripps and Comroe, Anesthesiology, 6: 462 (Sept.) 1945.

Cardiac Emergencies: 16 mgm. repeated as necessary was best for relief of pain in coronary occlusion. 15 mgm. injection relieved anxiety, cough, and dyspnea in acute left ventricular failure immediately. Griffith, M. Clin. North America, 27: 1531 (Nov.) 1913.

Eclampsia: Morphine was reliable and powerful, given in 0.02 to 0.4 gm. doses (average 0.08 to 0.1 gm.) Since convulsions did not occur if respiration was less than 11 to 16 per minute, treatment involved heavy sedation. Plass, J.A.M.A., 119: 872, 1912.

Intractable Pain: 15 mgm. every three to four hours was given. Total duration of threshold raising action was six to eight hours. SeEVERS, Wisconsin M. J., 41: 113; 1911.

Fatal Dose: Average fatal dose is about 0.005 gm/kg. Quercis and Minor Notes, J.A.M.A., 128: 985; 1945.

Delayed Poisoning: Subcutaneously, 0.03 gm. given to chilled patient with low blood pressure, caused dangerous respiratory depression and coma from sudden absorption. Lack of circulation did not allow drug to take effect, hence second dose was given in short time. *Treatment:* tourniquet was placed near site of injection to retard rate of absorption. Avoid poisoning by slow intravenous administration of not more than 8 mgm. Bull. U. S. Army M. Dept., 74: 5 (Mar.) 1944.

MUSTARD GAS

Guinea Pigs—

Cachexia: 20 mgm/kg. applied to skin caused maximal weight loss of 30 to 40% which alone caused death. Telbisz and Kucharik, Biochem. Ztschr., 307: 82; 1940.

Man—

Poisoning of Eye: Treated with three drops of 2.5% sulfacetamide in each conjunctival sac, repeated two and four hours later, followed by 2.5% sulfacetamide ointment between the lids twice a day for four days. Pupils dilated with atropine four days. Aitken, Lancet, 245: 602; 1943.

NEOARSPHENAMINE

Rats (white)—

Detoxication: Simultaneous administration of 0.5 mole ascorbic acid reduced toxicity of intravenous LD₅₀ of arsphenamine (450 mgm. was approximately one mole). Three moles of lactic acid were equivalent to 0.5 mole of ascorbic acid in detoxifying 450 mgm. of neoarsphenamine. McChesney, Barlow, and Klinck, J. Pharmacol. & Exptl. Therap., 80: 81 (Jan.) 1944.

Rabbits—

Experimental Syphilis: 98% cleared by intravenous injection of 10 mgm/kg. and a fever of 41.5° C. for three to four hours artificially induced by carbon filament lamps. Boak et al., Am. J. Syph., Gonor. & Ven. Dis., 26: 282 (May) 1942.

Man—

Amebiasis: Intravenously, 3 mgm. followed by 1.5 mgm. daily for four doses successfully treated intestinal amebiasis: Noel, Union méd. du Canada, 74: 1381 (Oct.) 1945.

Fusospirochetal Pulmonary Abscess: Four intravenous injections of 0.6 gm. doses in two weeks followed by 22 intramuscular injections of

0.6 gm. sulfarsphenamine in three months completely cleared a case. Wiese and Heiken, *Pennsylvania M. J.*, 49: 28 (Oct.) 1945.

Leukomelanoderma One injection of 0.6 gm. and six injections of 0.9 gm. per week caused dermatitis and 18 months later a malignant melanoma. Rothman and Felsher, *Arch. Dermat. & Syph.*, 52: 64 (July) 1945.

Syphilis of Lung in a woman was treated with eight injections of 0.6 gm. doses, and 16 injections of bismuth subsalicylate, 0.13 gm. each, over a period of six months, followed by a four months course of potassium iodide. *Pennsylvania M. J.*, 48: 791 (May) 1945.

Tropical Eosinophilia A total of five injections of 0.3 gm. each every other day to one patient, and another received 0.1, 0.3, 0.45, and 0.45 gm. at three to five day intervals. Hodes and Wood, *Am. J. M. Sc.*, 210: 288 (Sept.) 1945.

Tularemia: 0.6 gm. at weekly intervals plus serum. Werling, *J. Oklahoma M. A.*, 35: 103 (Mar.) 1942.

Vincent's Infection: 0.6 gm. arrested but did not clear infection in Australian natives due to vitamin C deficiency and betel nut chewing. Amies, *M. J. Australia*, 2: 275 (Sept.) 1945.

Yaws: 0.6 gm. intravenously, and 0.13 gm. bismuth subsalicylate intramuscularly, three times at four day intervals, then weekly, were given to a 20 year old white man 21 days after start of treatment, all lesions healed. Kinell, *U. S. Nav. M. Bull.*, 42: 187 (Jan.) 1944.

0.45 gm. initially, then 0.6 gm. per week were given, 12 injections in all. Average dose for clinical cure was 1.75 gm. de Wyt, *J. Roy. Army M. Corps*, 81: 255 (Dec.) 1913.

Liver Function Test. Hippuric acid liver function test during arsenotherapy detected impairment in detoxicating function of liver before onset of jaundice, and if done routinely, indicated when treatment should be stopped to avoid additional toxicity. Riddell and Anderson, *Lancet*, 246: 275; 1914.

Massive Arsenotherapy By intravenous drip, 1.5 gm. in 250 ml. of double-distilled water during four hours on each three successive days, then one week after last injection, 0.9 gm. in 10 ml. was injected. Spirochaetes disappeared in 24 hours. Prunes and Hevia, *Arch. Dermat. & Syph.*, 45: 891 (May) 1912.

By intravenous drip, 1.5 gm. in 300 ml. of physiologic saline was given daily for three days. Bryan, *Geneesk. tijdschr. v. Nederl. Indië*, 81: 2350; 1911; through *J. A. M. A.*, 118: 1336, 1912.

Sensitivity relieved with 50 to 100 mgm. of ascorbic acid daily, by oral administration in minor cases, and 100 mgm. crystalline ascorbic acid in each 10 ml. solution containing 0.6 gm. neoarsphenamine in severe cases Vail, J. Missouri M. A., 38: 110 (Apr.) 1941.

NEODYMIUM SALTS

Man—

Phlebothrombosis: Single intravenous injection of 4.5 to 12.5 mgm. neodymium salt per kilo produced definite anticoagulant effect. Peak reached within one hour and then decreased, which was prevented with successive smaller doses. Single 12 gm. dose increased clotting time two to four times, for over six hours. Toxic reactions were thrombophlebitis, at site of injection, headache, sweating, chills, fever, abdominal and muscular pain, nausea, vomiting, hemoglobinemia and hemoglobinuria. Other rare earth salts, lathanum acetate and cerium acetate in 1.6 to 5 mgm/kg. doses gave more severe reactions, therefore abandoned. Beaser, Segel, and Vandam, J. Clin. Investigation, 21: 447 (July) 1942.

NEOPRONTOSIL

(Disodium 7-acetamide-2-(p-sulfamylphenyl azo)-1-naphthol-3,6-disulfonate)

Man—

Pulmonary Abscess: 14 to 15 inhalations of an aerosol containing 5% neoprontosil in 25 ml. of distilled water or physiologic saline at 35° C. for five to six weeks caused complete regression in six patients. Moreno, Villaclara Med., 13: 125 (Mar.-Apr.) 1945.

Septic Sore Throat: 0.65 gm. every three hours for 24 hours, every four hours for next 24 hours, had marked bactericidal action on hemolytic streptococci. Coakley, Nebraska M. J., 27: 18 (Jan.) 1942.

NEOSTAM

(N-glucoside of sodium stibanilate)

Mice (white)—

Experimental Histoplasmosis: Intraperitoneally, 0.2 mgm. begun 24 hours after infection was of no value. Levy, Am. J. Trop. Med., 25: 241 (May) 1945.

Rats—

Filariasis: Intramuscularly, 40 to 60 mgm. caused microfilariae of *Litomosoides carinii* to disappear from peripheral blood seven to 64 days after fourth injection Culbertson and Rose, Science, 99: 245 (Mar.) 1944.

Hamsters (Syrian)—

Experimental Leishmaniasis Subcutaneously, 250 mgm/kg. significantly reduced number of parasites in spleen Goodwin, Tr. Roy. Soc. Trop. Med. & Hyg., 38, 151 (Nov.) 1944.

Man—

Leishman

0.3 g;

days, 1.85 gm. in doses not exceeding 0.2 gm. was given. After two months, sodium fo Distressing cough. 20
J., I 492 (Apr.) 1944.

NEOSTIBENE

Man—

Kala Azar Therapy: Intramuscularly, 0.1 gm. twice of 1.0 to 4 gm. Donovan b

1941.

J., 12, 158 (Dec.)

NEOSTIBOSAN

Hamsters (Syrian)—

Experimental Leishmaniasis. 165 mgm/kg. subcutaneously, significantly reduced number of parasites in spleen. Goodwin, Tr. Roy. Soc. Trop. Med. & Hyg., 38: 151 (Nov.) 1944.

Man—

Filariasis Therapy: Intravenously, 50 mgm. initially, increased to 300 mgm. in three injections on alternate days, 300 mgm. was given six days per week thereafter until end of treatment in 33 to 48 days. Culbertson, Rose, and Oliver-Gonzalez, Am J. Trop. Med., 25: 271 (May) 1945.

Cutaneous Leishmaniasis 12 biweekly injections of 5 ml. doses, intramuscularly or intravenously, gave successful results. Berberian, Arch. Dermat & Syph., 52: 26 (July) 1945

Visceral Leishmaniasis (kala azar) Treatment with 0.1 to 0.3 gm. on alternate days, and if no toxic reactions occurred, dose was increased and continued until a total of 3 gm. for each 45 kg was given. Queen, Northwest Med, 44 122 (Apr.) 1945.

Visceral Leishmaniasis 0.2 gm injected, followed by 0.3 gm. doses to a total of 3.8 to 5 gm. If reactions occurred, daily injections were changed to every other day. If parasites were present in fourth week, another course was given. Bull. U. S. Army Med Dept. 4, 296 (Sept.) 1945.

NEOSTIGMINE

Mice—

Anoxia: 0.2 mgm. bromide per kg. orally, and 100 mgm. diphenylhydantoin per kg. intraperitoneally minimized lethal effects of severe anoxia. Intraperitoneally, 0.3 mgm/kg., orally 0.5 mgm/kg. and intraperitoneally, 0.3 mgm/kg. with diphenylhydantoin resulted in 25, 5 and 15% mortalities, respectively, under normal atmospheric condition. Emerson, Proc. Soc. Exper. Biol. & Med., 54: 252 (Nov.) 1943.

Man—

Arachnidism. Intramuscularly, 2 ml. of 1:2000 methyl sulfate in combination with 0.4 mgm. atropine sulfate relieved muscle spasm and pain within one hour. Bell and Boone, J.A.M.A., 129: 1016; 1945.

Clinical Uses: Injection of 1 ml. methyl sulfate in simple amenorrhea and as an early diagnostic agent for pregnancy; 1 ml. methyl sulfate every other day for three to six doses and 15 mgm. of the bromide three times a day relieved back pain due to muscular spasm. Jones, Virginia M. Monthly, 72: 469 (Nov.) 1945.

Pre-eclamptic Patients: One to three intramuscular injections of 0.25 mgm. of the methyl sulfate at 90 minute intervals, followed by one to two hourly injections of 0.02 to 0.25 mgm. intravenously until uterine activity began and blood pressure fell. Uterine activity started after latent period of 90 to 120 minutes. Labor induced. Woodbury et al., J.A.M.A., 128: 585; 1945.

Intestinal Paralysis. 1 mgm. was given for patients weighing 57 kg. or heavier, less than 1 mgm. for lighter persons. Contraindicated in impending perforation of intestinal wall. Schwartz, Rheingold, and Necheles, Surgery, 11: 746 (May) 1942.

Myasthenia Gravis. Half of 45 patients maintained on 163.5 mgm every 24 hours; 36 of 43 also took 24 mgm. ephedrine sulfate three times a day. Viets, Lancet, 246: 33 (Jan.) 1944. Controlled by 31 mgm of the methyl sulfate in 24 hours; 3 mgm. in 1500 ml. of 5% glucose administered by continuous intravenous drip and the remainder intramuscularly 1.0 to 1.5 mgm. per hour. Orally, 525 mgm. bromide per 24 hours was gradually substituted Viets, Am J. M. Sc., 208: 701 (Dec.) 1944 Ambulatory cases treated with 0.5 mgm methyl sulfate (1 2000); and severe cases with 24 mgm. intramuscularly and 3 mgm. intravenously in 24 hours. Viets, Lancet, 246: 33 (Jan) 1944. 0.5 mgm. intramuscularly of methyl sulfate every two hours brought dramatic response to five year old child. On second day, oral neostigmine bromide was given every three hours; gradually

reduced; maintenance dose of 7.5 mgm every 12 hours was satisfactory. Lieberman, J.A.M.A., 120: 1209; 1942.

Muscular Dystrophy: Intramuscularly, 1 ml. 1:2000 solution twice weekly for six months completely regressed disease in 36 year old patient without relapse in two years Skaller, J. Arkansas M. Soc., 42: 94 (Oct) 1915.

Neuromuscular Dysfunction Improvement with subcutaneous injection of 1:2000 methyl sulfate solution with 0.6 mgm. or 0.4 mgm. atropine sulfate once or twice daily. Kabat, Pub. Health Rep., 59: 1635 (Dec.) 1944.

Parotid Duct Obstruction: Hypodermically, 1 ml. of 1:2000 methyl sulfate solution either once or twice eliminated distress and reduced salivary gland size in three patients Perner, Am J Digest Dis. & Nutrition, 9: 417 (Dec.) 1942.

Poliomyelitis: Subcutaneous doses of methyl sulfate were: adult, 1.5 mgm.; older children, 1.125 mgm., younger children, 0.5 mgm. Eveleth and Ryan, Yale J. Biol. & Med., 17: 351 (Dec.) 1914 Subcutaneously, 1 mgm. daily was given to 13 patients, orally 30 mgm. at 8:00 A.M. and 15 mgm. at 6:00 P.M. were given to 17 patients with variable results. Fox and Spankus, J.A.M.A., 128: 720, 1945

Subcutaneously, 0.5 mgm. of methyl sulfate to children under six, 1 mgm. to those between six and 12 years, and 1.5 mgm. to adults relaxed muscles within one hour in 85.7% of 28 patients Subcutaneous dose was supplemented with 15 to 45 mgm. of bromide orally, three times a day, plus Kenny method hot packs in some Recovery was 21.8 days for neostigmine alone, 51.7 days for those receiving hot packs as well. Average recovery with hot fomentations alone was 35.6 days Brainerd et al., J.A.M.A., 128: 718; 1945.

One to 2 ml. of 1:2000 solution twice a day was effective when given alone. McLendon et al., M. Ann. District of Columbia, 14: 287 (July) 1945.

Parenterally, 0.25 mgm. every two to three days and orally, 7.5 mgm. once or twice a day was given, while some required parenterally, 0.5 mgm. several times daily and orally, 14 to 30 mgm. three times a day for symptomatic relief Not used with curare, but each could counteract overdose of other. Orth, Wisconsin M. J., 44: 993 (Oct) 1915.

Pregnancy Diagnosis Intramuscularly, 1 ml. of a 1:2000 solution of methyl sulfate on three consecutive days produced normal menstruation in non pregnant, non menopausal patients Grossman, West J. Surg., 52: 413 (Oct.) 1914.

Rheumatoid Arthritis: 1 ml. of methyl sulfate 1:2000 (0.5 mgm.) subcutaneously daily and 0.6 mgm. atropine sulfate administered every other day. In addition, treatment consisted of 7.5 to 45 mgm. neostigmine bromide, orally, with 0.6 to 1.2 ml. tincture of belladonna daily. Trommer and Cohen, J.A.M.A., 124: 1237; 1944.

Serum Cholinesterase Inhibition: No direct relationship between clinical effect and serum cholinesterase inhibition followed administration of neostigmine alone or with ephedrine in myasthenia gravis. Subcutaneously, 1.5 mgm. caused 33 to 35% maximum inhibition; at 18 to 19% inhibition, clinical signs reappeared. Oral 15 mgm. caused maximum inhibition of 13% serum cholinesterase, during which there was no clinical improvement. Wilson and Stoner, Lancet, 246: 429; 1944.

NEOSYNEPHRIN

Man—

Dosage Levels: Threshold doses were 0.4 mgm. intravenously; 50 mgm. orally; and 2 mgm. subcutaneously. Average doses were: 0.8 mgm. intravenously; 250 mgm. orally; and 5 mgm. subcutaneously. Keys and Violante, J. Clin. Investigation, 21: 1 (Jan.) 1942.

NEPTAL

(o-hydroxy-mercuri-propanol-amido-carboxy-phenoxy-acetic acid)

Man—

Fatal: 2 ml. intravenously following an initial dose of 0.5 ml.; 2 ml. six times in 13 days; 23 days urea medication. Rennie, Lancet, 248: 53; 1945.

NICOTINAMIDE

Dogs—

Bioassay: Urinary elimination of purple or blue fluorescent substance as a basis for assaying foodstuffs. Measureable differences obtained with 0.4 to 2.0 mgm/kg. in dogs. Ferrets were convenient test animals. Ellinger, Glock, and Platt, Biochem. J., 36: xi (Sept.) 1942.

Man—

Glycemia: Orally or parenterally, 0.5 gm. produced in 14 of 18 a transitory 10 to 40% decrease in blood sugar, hyperglycemia in three, and ineffective in one. Marche and Belbarre, Compt. rend. Soc. de biol., 137: 153 (Mar.) 1943.

Lingual Atrophy: Orally, 50 mgm. per day for 19 weeks improved markedly in 17, no further improvement being effected with administra-

tion in following few months of 100 mgm. or 1 mgm. riboflavin daily. Sevringhaus and Kyhos, Arch. Int. Med., 76: 31 (July) 1945.

Muscular Effort: Acceleration of coordinated muscular effort by single dose of 200 mgm., effect being most marked one and one half to three hours after administration of vitamin I rankin, Brit. M. J., II 601 (Nov.) 1943.

NICOTINE

Mice and Rabbits—

Effect of Epinephrine: 1:1000 epinephrine solution failed to protect against fatal intoxication by nicotine sulfate (containing 2% nicotine base) whether nicotine was injected simultaneously with or two hours after epinephrine injection. Haag and Fisher, Am. J. Hyg., 35: 40 (Jan) 1942.

Dogs—

Fate: Subcutaneously, 0.2 mgm/kg in 2% solution was given to four female dogs. 10% was excreted unchanged in urine while remainder appeared in nicotinic acid fraction in urine. Larson and Haag, J. Pharmacol. & Exper. Therap., 76: 210 (Nov.) 1912.

NICOTINIC ACID

Rats—

Excretion: 120 gammas excreted on diet containing 5 gm. of protein, dropped to 90 gammas after five days of fasting. 25 to 75 gammas nicotinic acid derivatives were excreted in urine and 40 to 90 gammas in feces on protein free diet containing seven gammas nicotinic acid. Huff and Perlwig, J. Biol. Chem. 112: 101, 1912.

Rabbits—

Blood Calcium and Potassium: 10 mgm/kg increased potassium content with hypocalcemia. Fichera and Vasta, Biochim. e terap. sper., 28: 100; 1941; through Zschr. f. Vitaminforsch., 12: 161, 1942.

Carbohydrate Metabolism: Intravenously 10 mgm/kg produced hyperglycemia, reaching maximum in one hour and disappearing after two hours. Fichera and Vasta, Biochim. e terap. sper., 28: 97, 1941, through Zschr. f. Vitaminforsch., 12: 160, 1942.

Experimental Fractures (in young adult males): Administration of 0.05 gm. and 0.1 gm. every other day accelerated healing and stimulated formation of callus, and stimulated function of reticulo-endothelial cells, especially of liver and spleen. Scartozzi, Med. Sper. Arch. Ital., 6: 609 (Oct.) 1940, through J. A. M. A., 116: 1744, 1941.

Nitrogen: Two hours after 10 mgm/kg. was given, total and protein nitrogen decreased. Residual nitrogen decreased as early as one hour after administration. Fichera and Vasta, *Biochim. e terap. sper.*, 28: 104; 1941; through *Ztschr. f. Vitaminforsch.*, 12: 161; 1942.

Dogs—

Requirement: 200 to 225 gammas/kg. per day for adult dogs and 250 to 365 gammas for young growing dogs. Sulfapyridine inhibited curative action of nicotinic acid, nicotinamide, dried liver and liver extract powder in dogs suffering from nicotinic acid deficiency. Overcame with fresh liver. Schaefer, McKebbin, and Elvehjem, *J. Bio. Chem.*, 144: 679 (Aug.) 1942.

Swine—

Enteritis: 100 to 300 mgm. orally had no effect on experimental infection of *Salmonella cholerae suis* enteritis. Edgington et al., *J. Am. Vet. M. A.*, 101: 103 (Aug.) 1942.

Man—

Allergy (seasonal): Hypodermically, 50 mgm. per day for relief. Shea, *Laryngoscope*, 55: 325 (July) 1945.

Angina Pectoris: Orally, 10 to 50 mgm. daily reduced number of attacks. Not as effective as nitrites in relieving attack of anginal pain nor in preventing its pain. Value lay in reduction of frequency, attributed to vasodilatation. Moncrieff, *Lancet*, 242: 633 (May) 1942.

Asthmatic Paroxysm: Intravenously, 0.1 gm. controlled in 16 of 21 patients. Relief in three to five minutes after injection. 18 of these, given 0.2 gm. orally before meals, and on retiring, showed improvement in asthma. Maisel and Somkin, *J. Allergy*, 13: 397 (May) 1942.

Deficiency Test: After 500 mgm. orally or intravenously, average 12 hour excretion for normal adults, undernourished boys, and hospital cases were 7.3, 1.9, and 2.7 mgm. Twelve hour excretions before administration for similar group were: 0.9, 0.8, and 0.7 mgm., respectively. Perlweig, Sarett, and Margolis, *J.A.M.A.*, 118: 28; 1942.

Dermatitis: 50 to 1000 mgm. cleared up dermatitis manifestation of pellagra. Novy, *California & West. Med.*, 56: 144 (Mar.) 1942.

Digestive Disorders: 600 mgm. daily abolished symptoms of anorexia, dyspepsia, and diarrhea. Gueffroy and Lucc, *Munchen. med. Wchnschr.*, 88: 159; 1941.

Electrocardiograph Changes: Female pellagrin received orally, 500 mgm. per day. Six days later, "T"-waves showed slight depression, in-

stead of former inversion Male pellagrin treated with 500 mgm. orally, and 100 mgm. intravenously, per day improved in six days. Rachmilewitz and Braun, *Am Heart J*, 27: 203 (Feb.) 1944.

Glossitis: Intramuscularly, 200 to 300 mgm. daily produced response in five patients. Ghalioungui and Jalily, *Lancet*, 249: 352; 1945.

Headache: Relief with 25 mgm. hypodermically, repeated in 20 to 30 minutes. Injections were given every other day, and interspaced with 50 to 100 mgm. orally. Shea, *Laryngoscope*, 655-325 (July) 1945.

Levels: 0.24 mgm.% to 0.515 mgm.% were levels in aged persons, having no correlation to general health. 300 mgm. daily raised level to 0.2 to 0.3 mgm.% in three weeks Chutuck and Stolz, *Dis. of Nervous System*, 2: 71 (Feb.) 1941.

Cerebral Malaria: Consciousness regained in 35 minutes after intravenous administration of 200 mgm./0.5 liter of saline. Dhillon, Joshi, and Roy, *J. Roy. Army M. Corps*, 84-268 (June) 1945.

Malaria Headaches: Orally, 50 to 100 mgm. taken before breakfast gave relief for entire day. Zeligs, *J. A.M.A.*, 129: 796; 1945.

Menière's Syndrome. Migraine treated with 30 mgm. intramuscularly, followed by six or eight intravenous injections two to three times weekly, increasing initial dose by 5 mgm. to maximum of 50 mgm. Orally, 50 to 150 mgm. daily was also given Atkinson, *J. M. Soc. New Jersey*, 41: 11 (Jan.) 1944. Parenterally, initial dose of 25 mgm. followed by increasing doses until 100 mgm. was reached, relieved symptoms in 50 of 62 patients. Williams, *Proc. Staff Meet., Mayo Clin.*, 20: 373 (Oct.) 1945.

Nausea and Vomiting (pregnancy) 50 mgm. three times daily. Hart, Sydenstricker, and Torpin, *Bull. Univ. Hosp. (Georgia)* 3: 11 (Dec.) 1941.

Nutritional Diarrhea: Injection of 50 to 100 mgm. daily controlled diarrhea in 12 days in 50 patients. Editorial, *Brit. M. J.*, II: 258 (Aug.) 1945.

Optic Neuritis: 300 mgm. daily in five cases brought rapid improvement in first ten days of treatment Barracnechea et al., *Ophth. Iber. Am.*, 5: 7 and 21; 1943; through *Am. J. Ophth.*, 27-91 (Jan.) 1944.

Pellagra: 100 to 1000 mgm. daily, 60 to 125 mgm. four times daily by mouth. Schroeder and Driantoff, *Deutsche med. Wchnschr.*, 67: 726 (July) 1941; through *J.A.M.A.*, 118-177, 1942 Orally, 600 mgm. and 300 to 400 mgm. intramuscularly or intravenously, plus riboflavin 3 mgm. (minimum daily therapeutic dose), most patients required 5 mgm. Sydenstricker, *Ann. Int. Med.*, 14: 1499 (Mar.) 1941.

Rheumatoid Arthritis: By intravenous drip, 200 ml. of 0.05% solution, if tolerated, a daily intravenous dose of 400 ml. of 0.05% for three to four weeks during hospitalization. Additional three doses of 50 mgm. each was given orally at 15 minute intervals on empty stomach, two or three times daily. Promising results obtained in 36 patients. Kurtz, Orth, and Sepulveda, Wisconsin M. J., 44: 761 (Aug.) 1945.

Skin Lesions in diabetics treated with 150 to 300 mgm. per day orally, for a few days to several months. Rudy and Hoffmann, New England J. Med., 227: 893 (Dec.) 1942.

Cerebral Thrombosis: With 5 to 10 mgm. intravenous injections, three cases showed regression of symptoms of a recent hemiplegia within a few hours. Furtado, Lancet, 242: 602; 1942.

Vincent's Angina: Adult dose: orally, 50 mgm. three times a day for one week; child's dose: 10 mgm. or more according to age. Temperature subsided in 48 to 72 hours, and smears were negative in four to seven days. Johnson, J.A.M.A., 129: 91; 1945.

Anesthetic Vomiting: 50 mgm. preoperatively and then postoperatively slightly reduced incidence of vomiting. Mushin and Wood, Brit. M. J., I: 719 (May) 1944.

Vincent's Ulceration: 1050 to 2100 mgm. had favorable effect on six of 15 patients. Proc. Roy. Soc. Med., 37: 567 (Aug.) 1944.

Habitual Vomiting of nursing infants: 15 mgm/kg. two to three times daily was given. Virassoro and Monsoliu, Prensa méd. argent., 30: 292; 1943; Biol. Abst., 17: 20056 (Oct.) 1943.

Urticaria: 20 mgm. twice daily and 5 gr. calcium lactate three times a day with meals cleared in three to four days. Continued 10 mgm. daily for ten days then every two days for one month. Chambers and Bernton, J. Allergy, 15: 141 (Mar.) 1944.

NICOTINIC ACID AND RELATED COMPOUNDS

Man—

Intracranial Blood Flow: Intravenously, 20 to 50 mgm. nicotinic acid caused increased and persistent blood flow, flushed skin, but no arterial blood pressure change. Intravenously, 42 mgm. quinine nicotinate definitely increased intracranial blood without change in arterial blood pressure. Intravenous injection of 50 to 75 mgm. nicotinic acid amide had no effect Aring et al., Arch. Neurol. & Psychiat., 46: 649 (Oct.) 1941.

NIKETHAMIDE

Man--

Cerebral Malaria: Intravenously, 3 ml. every 30 minutes, and 0.8 gm. quinine dihydrochloride in 0.26 gm. doses every four hours caused recovery of consciousness in less than 24 hours in one patient. Dhillon, Joshi, and Roy, J. Roy. Army M. Corps, 84: 268 (June) 1945.

Shock Therapy: Intravenously, 10 ml. restored muscular tonus within five to ten minutes and maintained clinical improvement for two hours in patients whose peripheral circulation had failed due to shock. Cough reflex followed by mild convulsive movements of extremities indicated maximum toleration. No contraindication, toxicity was low. In severely shocked patient, 30 ml. intravenously in 30 minutes produced good results. Gunther, U. S. Nav. M. Bull., 44: 300 (Feb.) 1945.

Visual Acuity: Two hours after 3 ml. was given, average improved from 20/17.2 to 20/15.9 in men 17 to 40 years old, and reading speed improved from 0.358/letter to 0.274/letter. Lebensohn and Sullivan, U. S. Nav. M. Bull., 43: 90 (July) 1945.

NITROGEN OXIDES

Rats, Mice, Guinea Pigs, Rabbits, Cats--

Toxicology: Exposures to concentrations from 30 to 1000 parts per million, expressed as gaseous nitrous oxide, at 25° C. and 760 mm., caused death in 84 to 112 animals (88% from lung edema, 6% from asphyxia, and 6% from pneumonitis). La Towsky, MacQuiddy, and Tollman, J. Indust. Hyg. & Toxicol., 23: 129 (Apr.) 1941.

Guinea Pigs--

Toxicity: 30 parts per million for three hours was harmless. Ibid.

Guinea Pigs, Rabbits, Cats--

Toxicity: Exposure to 55 parts per million had no effect, but 100 parts per million was not tolerated. Ibid.

NITROGLYCERINE

Man--

Angina Pectoris: 0.6 mgm. tablet under the tongue relieved pain as promptly as and more conveniently than 3 minims of amyl nitrite. Griffith, M. Clin. North America, 27: 1531 (Nov.) 1943.

Acute Poisoning: Symptoms described, prevention given. Treatment not satisfactory, but helped by strong coffee, caffeine, and sodium benzoate (0.5 gm.) intravenously, or a cold cloth or ice to the head. Rabinowitch, Canad. M. A. J., 50: 199 (Mar.) 1944.

NUPERCAINE

(2-butoxy-N-(β -diethylaminoethyl) cinchoninamide)

Mice (white)—

Toxicity: M.L.D. was 30 mgm/kg. intraperitoneally. Co Tui et al., *Anesth. & Analg.*, 22: 301; 1943.

Rabbits—

Toxicity: Intraspinal minimal lethal concentration was 2.4% in unpremedicated animals. Co Tui et al., *J. Pharmacol. & Exper. Therap.*, 75: 137 (June) 1942.

Cats—

Toxicity: Intraspinal minimal lethal concentration was 2.5% in animals premedicated with pentobarbital sodium. *Ibid.*

Man—

Convulsions caused by intercostal injection of 30 mgm. in 0.1% solution and 100 mgm. in 0.2% solution in woman anesthetized by inhalation. Waters, *Anesthesiology*, 6: 416 (July) 1945.

OCTACAINE

(2-methyl-2 (α -methylheptylamino) propyl p-aminobenzoate hydrochloride)

Mice (white)—

Toxicity: M.L.D. was 85 mgm/kg. intraperitoneally, and 184 mgm/kg. subcutaneously. Co Tui, *Anesth. & Analg.*, 22: 301; 1943.

Guinea Pigs—

Toxicity. M.L.D. was 95 mgm/kg. subcutaneously. *Ibid.*

Rabbits—

Pharmacology: M.L.D. was 12 mgm/kg. intravenously. Corneal anesthesia was obtained with 0.5 ml. of 1% solution in ten seconds, and lasted for 178 minutes. Injection of 0.2 ml. of 0.02% solution caused sciatic nerve block in 300 seconds and lasted 12.5 minutes. 1% solution induced anesthesia in 30 seconds and lasted 174 minutes. *Ibid.*

OCTOFOLLIN

(p,p'-(1,2-diethyl-3-methyltrimethylene) bis phenol)

Man—

Dose: Average dose is 2 to 3 mgm. in tablet form, or 2 to 5 mgm. by injection. 1 mgm. is equivalent to approximately 25,000 international units (or 1250 rat units) estrone. Council on Pharm. & Chem., *J.A.M.A.*, 124: 647; 1944

Action: Orally, 1 to 10 mgm. per day or intramuscularly, 2 to 5 mgm. in sesame oil given one to three times per week, relieved 73 with menopausal symptoms, six of seven with menorrhagia, 13 of 15 patients with pluriglandular dysfunction, six of eight with severe migraine headaches, two of five with senile vaginitis, and two with acute mastitis. There were no reactions; no nausea, vomiting, dizziness, headache, etc. **Effect of Thyroid:** 5 mgm octofollin alone per day was required for abolition of menopausal symptoms, but only 1.0 to 2 mgm. octofollin plus thyroid. **Lactation Suppression.** 5 to 10 mgm. given four times a day produced satisfactory results. **Gonococcus vaginitis:** Vaginal inserts containing 0.5 mgm octofollin were as effective as 1 mgm tablets or 1 mgm suppositories in 30 girls. Prompter cure, no secondary sex characteristics induced. Jaeger, J. Indiana M. A., 37: 117 (Mar) 1944.

OUABAIN

Cats—

Toxicity: Mean lethal dose in animals anesthetized with sodium pentobarbital or a combination of urethane and chloralose was 0.099 and 0.119 mgm/kg., respectively. Injection caused 20% decrease in frequency of sinus rate; infusion with 15% of lethal dose slowed heart rate; and infusion with 60% of lethal dose caused irregularity of heart rate. Krueger and Unna, J. Pharmacol & Exper. Therap., 76: 282 (Nov) 1942.

Dogs—

Extrasystoles caused by subapical injection of 0.1% solution and persisted for 22 minutes. Scherf, Exper. Med & Surg., 2: 70 (Feb.) 1944.

Man—

Congestive Heart Failure. Intravenously, five cat units in 10 ml., 10% dextrose solution was given, followed by four cat units digitalis, orally. Maintenance dose (1 cat unit) was started in second 24 hours. Smith, M. Times, New York, 70: 43, 1942.

OXALIC ACID

Man—

Hemophilia Intravenously, 10 to 27 mgm. daily did not reduce coagulation time in five cases. Johnson, Proc Soc Exper Biol & Med., 46: 496 (Mar.) 1941.

Hemostatic Effect 20 to 40 mgm., given intravenously or intramuscularly, to 440 operative patients with major surgery, was successful. Blain and Campbell, Arch Surg., 44: 1117 (June) 1912

OXOPHENARSINE HYDROCHLORIDE

Man—

Lupus Erythematosus: Intravenously, 0.02 gm. in 4 ml. of distilled water, an average of ten biweekly injections, benefited 21 cases. Goldberg, Arch. Dermat. & Syph., 52: 89 (Aug.) 1945.

Syphilis: Injections of 100 mgm. twice daily for six days produced 85 of 206 probable cures in early syphilis, and three injections of 40 to 60 mgm. and one injection of 0.2 gm. bismuth weekly for ten weeks produced 24 of 30 probable cures in secondary syphilis. Trow and Dixon, Arch. Dermat. & Syph., 52: 155 (Sept.) 1945.

OXYTOCIN

(See pitocin, p. 242)

Rabbits—

Blood Pressure: Ten oxytocic units per kilo caused average transient decrease in blood pressure of 130/95 to 50/43 mm. Hg in eight of 11 morphinized animals. Woodbury and Abreu, Am. J. Physiol., 142: 114 (Aug.) 1944.

OZONE

Aerial Disinfectant—

0.04% inactivated *Streptococcus salivarius*, *Streptococcus "C"* and *Staphylococcus albus*, when present as unprotected aerosol particles in atmosphere of 60 to 90% relative humidity, but not with protective coating of organic matter. Elford and Ende, J. Hyg., 42: 240 (May) 1942.

PALUDRINE

(1-(p-chlorophenyl)-5-isopropylbiguanide acetate)

Man—

Acute Benign Tertian Malaria: 10 to 100 mgm. every 12 hours for 14 or 28 days with high fluid intake clinically cured malaria as effectively as quinacrine. Vomiting 30 to 60 minutes after administration of drug and epigastric pain were occasionally seen. Plasma concentration, with 50 or 500 mgm. every 12 hours for 14 days, rose to 400 micrograms per liter on fourth and fifth day with higher dose. Adams et al., Ann. Trop. Med., 39: 225 (Dec.) 1945.

Malignant Tertian Malaria: Dosage as low as 50 mgm. every 12 hours for 14 days was effective in controlling clinical attacks; 200 mgm. and 500 mgm. similarly distributed have been used. Asexual parasites disappeared from blood in one to four days, and temperature became normal within four days; sexual forms did not disappear. Maegraith et al., Ann. Trop. Med., 39: 232 (Dec.) 1945.

PAMAQUIN

Man—

Intoxication: 0.32 gm in 24 hours, given the day after completion of a course of atabrine was followed by nausea, vomiting, and hemoglobinuria in 24 hours and in collapse in 48 hours. Responded to two liters of 10% glucose intravenously, per day, oral fluids to maintain daily urinary output of three liters, 0.5 gm choline three times a day, and transfusion of two liters whole blood. Nadler and Crawford, New Orleans M. & S. J., 98: 91 (Aug.) 1945.

PANCREATIC EXTRACT

(Depropanex)

Man—

Dysmenorrhea: Intramuscularly, 1.5 ml. deproteinated extract completely relieved menstrual pain within 15 minutes in 72 of 104 treatments given to 56 cases. Grossmann, Am. J. Obst. & Gynec., 50: 411 (Oct.) 1945.

Urolithiasis: Intramuscularly, 3 to 5 ml. for a maximum of ten doses (1 ml. = 10 depressor units) produced complete, slight and no relief of pain in 12, three, and five patients with urolithiasis, respectively. Reactions were mild, transitory pain at injection site, and in two patients one minute of blanching of face, dizziness, and faintness immediately after injection. Kirwin, Lowsley, and Menning, J. Urol., 51: 132 (Feb.) 1944.

PANTOPAQUE

Man—

In Venous System. 3 ml. used in myelographic examination entered inferior vena cava, but there was no evidence of oil embolus and toxic reactions were slight. Hinkel, Am. J. Roentgenol., 54: 230 (Sept.) 1945.

PANTOTHENIC ACID

Bacteria—

Assay: New method for simultaneous assay of pantothenic acid and β alanine which involves determination of both substances with yeast, determination of pantothenic acid with *Streptobacterium plantarum* and calculation of β -alanine as the difference. Nielsen, Hartelius, and Johansen, Naturwissenschaften, 31: 550 (Nov.) 1943.

Chicks (Single Comb White Leghorn)—

Requirement. 500 to 550 micrograms per 100 gm. of feed prevented dermatosis; 600 micrograms per 100 gm. of feed caused maximum growth. Bauernfeind, Norris, and Heuser, Poultry Sci., 21: 142; 1942.

tween intravenous injection of papaverine hydrochloride and sudden deep inspiration which interrupts usual phase of respiration. Range of values for fifty was 15.4 to 27.0 seconds (average 20.8 seconds). Papaverine circulation time was prolonged in patients with heart failure and shortened in hyperthyroidism. Elek and Solarz, *Am. Heart J.*, 24: 821 (Dec.) 1942.

Intravenously, 40 mgm. in 1.0 to 6 ml. solution gave unsatisfactory results in 50 patients, giving good end points in only 26%. Berk and Sapeika, *Am. Heart J.*, 30: 365 (Oct.) 1945.

Deaths: Intravenously, 0.03 and 0.065 gm. respectively, were fatal in five minutes in two patients. Sagall and Dorfman, *New England J. Med.*, 233: 590 (Nov.) 1945.

PARALDEHYDE

Mice (Swiss albino)—

Metabolism: Pulmonary excretions of oral 0.05 gm. to 1.0 gm/kg. and intraperitoneally, 0.025 to 0.5 gm/kg. were determined on normal and liver damaged animals (carbon tetrachloride, 1 mgm/kg. subcutaneously, 24 hours before paraldehyde). Blood concentration and tissue contents were determined after 0.25 gm/kg. was given intraperitoneally. Hitchcock and Nelson, *J. Pharmacol. & Exper. Therap.*, 79: 286 (Dec.) 1943.

Rats—

Median Lethal Dose: of 1:10 solution was 15.5 to 18 ml. for one to two months' animals; 13.75 to 16 ml. for two to three months' animals; 13.75 to 15 ml. for those of three to twelve months; and 12.5 to 13.5 ml. for animals over twelve months. Phillips, Carmichael, and Kay, *Anesthesiology*, 5: 287 (May) 1944.

Intraperitoneal Toxicity: 13.75 ml. to 14.5 ml/kg. was average lethal dose for animals weighing 105 gm. to 197 gm., and 13.5 ml. to 13.75 ml/kg. for those weighing 200 to 525 gm. Phillips, Carmichael, and Kay, *Fed. Proc.*, 1: 67; 1942.

Guinea Pigs—

Intraperitoneal Toxicity Minimum lethal dose of a 1:10 solution was 12.5 ml/kg and average lethal dose was 13 ml/kg. Kay, Carmichael, and Phillips, *Fed. Proc.* 1: 46; 1942.

Median Lethal Dose: 11.75 to 12.25 ml/kg. for animals weighing 280 to 499 gm., and 11.25 to 12 ml/kg for those in 500 to 1130 gm. group when determined on 316 normal animals using 11.75 to 13 ml. of 1:10 solution per kg. Kay, Carmichael, and Phillips, *Anesthesiology*, 5: 182 (Mar.) 1944.

Repeated Administration. After three intraperitoneal administrations of 10 ml. of 1:10 solution per kilo per week for four weeks, average weight dropped from 499 to 469 gm., average time for onset of sleep varied from 85 to 120 seconds; duration of sleep dropped from 95 to 31 minutes; and length of hypnosis dropped from 231 to 167 minutes. Carmichael, Kay, and Phillips, *Proc. Soc. Exper. Biol. & Med.*, 55: 22 (Jan.) 1944.

Rabbits—

Dosages: Minimum anesthetic dose was 0.3 ml/kg. at 0.5 ml. per second, given intravenously, and LD_{50} was 0.45 ml/kg. Burstein and Rovenstine, *Proc. Soc. Exper. Biol. & Med.*, 48: 669 (Dec.) 1941.

Cats—

Dosages: Minimum anesthetic dose was 0.3 ml/kg. at 0.5 ml. per second, given intravenously, and LD_{50} was 0.45 ml/kg. with massive pulmonary hemorrhage and dilatation of right heart. *Ibid.*

Dogs—

Dosages: Minimum anesthetic dose was 0.3 ml/kg. at 0.5 ml. per second intravenously, and LD_{50} was 0.5 ml/kg. *Ibid.*

Man—

Eclampsia. Rectally, initial dose of 37 ml. in 18 to 22 ml. of olive or mineral oil, repeated as restlessness returned. 41 to 55 ml. to maximum of 444 to 481 ml. over a three to four day period was given. Douglass and Linn, *Am. J. Obst. & Gynec.*, 43: 844 (May) 1912.

Confusional Mental States: 7.4 to 14.8 ml. in milk encouraged normal sleep. Great Britain War Office—Army M. Dept. Bull. #24, 1 (June) 1913; through Bull. War Med., 4: 101 (Oct.) 1913.

Deaths. 31 ml. in obstetrical analgesia, death followed caesarean operation. Kotz et al., *J. A. M. A.*, 110: 2145, 1938. Questioned validity of death attributed to paraldehyde. Speert, *J. A. M. A.*, 118: 66; 1912.

12 ml. in 6 ml. benzyl alcohol resulted in cyanosis, dyspnea, convulsions, and death. Infant died shortly after birth. Shoor, *J. A. M. A.*, 117: 154; 1911.

Obstetrics: Intramuscularly, 10 ml. was effective in ten minutes and lasted for three to four hours. Rectally, 11 to 15 ml. was given, and once patient was anesthetized intramuscular dose was given if more time was required. Mitchell, *Brit. M. J.*, 1: 718 (June) 1912.

Paraldehyde orally, considered obstetric analgesic of choice. 0.1 to 0.1 gm. phenobarbital, followed after a short interval by 14.8 to 22 ml. paraldehyde mixed with equal amount of aromatic elixir produced complete amnesia in 95%. Dean, *Anesth. & Analg.*, 22: 322 (Nov.) 1913.

Uses: Per rectum, 32 ml. doses, repeated if necessary in mental cases.

Oral administration not recommended for patients with pneumonia or bronchitis. Contraindicated in acute nephritis. Usual dosage was 3.7 to 7.5 ml. (up to 22 ml. safely given). 7.5 to 11 ml., twice or three times a day, was given for acute excitement. Fisher, Practitioner, 152: 108 (Feb.) 1944.

Determination—

Blood: Color reaction with *p*-hydroxy-diphenyl in sulfuric acid. *Tissues and Expired Air:* Polymerization to acetaldehyde in hot dilute sulfuric acid and absorption of liberated acetaldehyde in sodium bisulfite, followed by iodometric titration. Hitchcock and Nelson, J. Pharmacol. & Exper. Therap., 79: 281 (Dec.) 1943.

PARATHYROID EXTRACT

Dogs—

Experimental Hypoparathyroidism: 50 or 100 units per kg. doses elevated serum calcium for about five days during which time normal serum calcium levels of about 9 mgm.% prevailed for two to three days. McChesney and Giacomino, J. Clin. Investigation, 24: 680 (Sept.) 1945.

Man—

Peptic Ulcer: Acute, subacute, and most chronic ulcers improved on a bland diet and parathyroid administration of 1.0 ml. every three days for three doses, 0.6 ml. every five to seven days for six to twelve doses as required, then a small dose every two to three months to prevent recurrence. Crabb, J. Kansas M. Soc., 44: 368 and 373 (Nov.) 1943.

PAREDRIINE

(Parahydroxyphenylisopropylamine)

Man—

Action: 1/500 activity of epinephrine and two to three times activity of ephedrine in respect to cardiac standstill; long acting, stable sympathomimetic, active on oral administration. 40 to 60 mgm., three to four times daily, lessened tendency to cardiac standstill. Produced a definite sustained rise in arterial blood pressure, systolic pressure being influenced more than diastolic. Strong mydriatic. Nathanson, California & West. Med., 57: 301 (Nov.) 1942.

Blood Specific Gravity and Volume: 20 to 40 mgm. subcutaneously did not affect blood volume nor specific gravity, though blood pressure was increased. Engelberg and Nathanson, Proc. Soc. Exper. Biol. & Med., 51: 242 (Nov.) 1942.

Pressor Effect: Subcutaneously, 20 mgm. or 40 to 80 mgm. orally, had definite pressor effect on postoperative patients. Systolic pressure was

more affected than diastolic. Complete utilization on oral administration; marked individual variation. Nathanson and Engelberg, *Proc. Soc. Exper. Biol. & Med.*, 51: 239 (Nov.) 1942.

Rheumatic Heart Orally, 60 mgm. every two hours obtained good results in a patient with complete heart block, discontinued when 1320 mgm. were given due to auricular fibrillation. Later, doses ranging from 500 to 1400 mgm. daily were given for 26 days. Greene and Bennett, *Am. Heart J.*, 30: 415 (Oct.) 1945.

PAREGORIC

Hens, Rats, Guinea Pigs, Rabbits, and Cats—

Expectorant Action. 0.5 to 5 ml per kg., given by stomach tube, increased respiratory tract fluid output for three to four hours. Effect was marked in rats. Boyd and MacLachlan, *Canad. M. A. J.*, 50: 338 (Apr.) 1944.

PARENAMINE

(Casein acid hydrolysate and 1% d,l-tryptophane)

Man—

Nitrogen Balance: Intravenously, 60 to 90 gm in 700 ml. sterile 5% dextrose or isotonic sodium chloride solution, given at rate of 350 ml. per hour per day for four to 26 days effected positive nitrogen balance in 13 of 14 cases with destructive lesions of esophagus or stomach. Kozoll, Hoffman, and Meyer, *Arch. Surg.*, 51: 59 (July) 1915.

PATULIN

Chick Embryo Hearts—

Growth was prevented by 1 200 to 1 10,000 dilution Broom et al., *Brit. J. Exper. Path.*, 23: 195 (Dec.) 1911.

Mice—

LD₅₀: 0.5 to 0.7 mgm per 20 gm. *Ibid.*

LD₁₀₀: 12.5 mgm pure patulin per 20 gm Karrow and Foster, *Science*, 99: 265; 1911.

Rats—

Toxicity: LD₅₀ was 1.5 to 2.5 mgm. per 100 gm. when given orally, intravenously, intraperitoneally, or subcutaneously in increasing order of toxicity. Pulmonary hemorrhage and edema were main toxic reaction, but local inflammation, edema of subcutaneous tissue, hemorrhage of kidneys, pale and flaccid spleens and right sided cardiac failures were found. Broom et al., *Brit. J. Exper. Path.*, 23: 195 (Dec.) 1911.

Rabbits—

Diuresis: Subtoxic doses caused antidiuresis; over 2.5 mgm. abolished diuresis. Ibid.

PAVATRINE

(β -diethylaminoethyl-9-fluorene-carboxylate hydrochloride)

Man—

Air Sickness: 0.13 to 0.26 gm., given ten minutes to one and a half hour before, produced no abnormal reactions to conditions of anoxia or high altitude. Davidson, J. Aviation Med., 15: 141 (Apr.) 1944.

PECTIN**Dogs—**

Post-hemorrhagic Hypotension: 1.5% buffered pectin solution, exerting an oncotic pressure of 67 to 68.7 cm. of water, was injected at a rate of three to five ml. per minute at varying periods of hypotension (50 mm. Hg). It was useful at early period of hypotension. Given after 30 minutes, 11 of 19 animals showed satisfactory hemodynamic response for four to six hours after administration. Middleton and Wiggers, Am. J. Physiol., 140: 326 (Dec.) 1943.

Man—

Plasma Volume: Intravenously, 0.75% in 690 ml. amounts, given to five patients with normal cardiovascular systems produced sustained rise in plasma value. Jacobson and Smyth, Proc. Soc. Exper. Biol. & Med., 50: 218 (June) 1942.

Poliomyelitis: 20 ml. of 3% pure pectin solution administered to gluteal region had favorable effect on intestinal disturbance and disease. Brunthaler, Monatschr. f. Kinderh., 88: 53 (May) 1941; through J.A. M.A., 119: 847; 1942.

Shock Therapy: 1.5% pectin in Ringer's or sodium chloride solution, buffered with sodium phosphate or sodium lactate to approximately pH 7.2 before administration. Infusion of 1 liter permanently relieved shock. Meyer et al, Surg., Gynec. & Obst., 78: 327 (Mar.) 1944.

PENICILLIN**In Vitro—**

Stability: 100 units/ml. 50% inactivated in 16 minutes at 24° C. and pH 2.0, but with pH 5.0, similar inactivation took four to five days. Irreversible. Benedict and Schmidt, J. Bact., 47: 425 (May) 1944.

Assay Methods—

Four hour turbidimetric method. Joslyn, Science, 99: 21; 1944.

Gutter plate method, double ditch plate, agar cup method, filter paper method, and Petri dish cell technic. Lumb and Wilson, J. Roy. Army M. Corps, 84: 247 (June) 1945.

"Depth test method." Brodie, J. Path. & Bact., 57: 257 (Apr.) 1945.

Ability of penicillin to inhibit hemolysin production by *Streptococcus pyogenes*, permitting readings in 55 to 90 minutes. Rake and Jones, Proc. Soc. Exper. Biol. & Med., 54: 189 (Nov.) 1943.

Guinea Pigs—

Experimental Rocky Mountain Spotted Fever: Intramuscularly, massive doses of 500 units every four hours (48 hours after onset of fever) for four days for a total of 12,000 units had no effect. Fitzpatrick, Science, 102: 96 (July) 1945.

Rabbits—

Hemorrhage: Produced at site of injection within two hours by 6,000 units in 0.5 ml. volume. Putnam et al., J.A.M.A., 127: 217; 1945

Lung Instillation. 1.0 to 3.0 ml. in iodized oil injected through trachea into bronchi. (1 ml. = 1,500 units). Blood levels of 0.39 to 1.25 units were found 15 and 30 minutes, and one and two hours later, depending on amount instilled. After two months when animals were sacrificed, no organ abnormalities were noted. Romansky, Dugan, and Rittman, Science, 102: 255; 1945.

Monkeys—

Convulsions: Injection into motor cortex of 0.05 ml. of a solution containing 2000 Oxford units/ml. was followed by generalized convulsions and unilateral fits, and 0.05 ml. containing 250 units/ml. provoked unilateral fits in one of ten animals. Walker, Johnson, and Kollros, Surg., Gynec. & Obst., 81: 692 (Dec.) 1945.

Man—

Absorption: Equal in subcutaneous and intramuscular administrations. Effective blood levels in ten minutes to three hours. Cook and Goldring, J.A.M.A., 127: 80, 1945.

Allergic Reaction: Intramuscularly, 20,000 Oxford units every three hours caused development on the fifth day a generalized urticaria accompanied by severe peri-articular arthralgia and hyperpyrexia was preceded by a punctate pruritic eruption. Price, Canad. M. A. J., 53: 485 (Nov.) 1945.

Allergy: Gonorrheal ophthalmia cleared with 500 units per ml. instillations of four drops per hour. Allergy occurred if instillation was pro-

longed beyond 24 hours. Vorisek, J.A.M.A., 126: 622; 1944.

Blood Level: Was highest 30 minutes after subcutaneous or intramuscular injection, and detectable up to eight hours later. Cook and Goldring, J.A.M.A., 127: 80; 1945.

Death occurred in two infants under two months given to 40,000 units per kilo every four hours for eight days. Lentz et al., J.A.M.A., 126: 408; 1944.

Dermatitis: Two physicians, during administration, developed eruptions within a few weeks of first contact. Patch test was positive in one; both recovered when contact was discontinued. Binkley and Brockmole, Arch. Dermat. & Syph., 50: 326 (Nov.) 1944.

Research chemist developed itchy rash of eyelids and penis. Patch test was positive for amorphous penicillin, and negative for crystalline. Cleared with avoidance of direct contact. Silvers, Arch. Dermat. & Syph., 50: 328 (Nov.) 1944.

Produced by contact with solutions and by administration. Patch tests proved diagnostic. Pyle and Rattner, J.A.M.A., 125: 903; 1944.

Herxheimer Syndrome occurred 18 hours after 100,000 units were given in one case, and shortly after intramuscular injection of 20,000 units in another. Bauer and Egolf, Bull. U. S. Army M. Dept., 4: 239 (Aug.) 1945.

Occurred four hours after treatment of yaws with 20,000 units of sodium salt, intravenously, and 15,000 units intramuscularly, followed by 15,000 units every three hours. Lofgren, U. S. Nav. M. Bull., 43: 1025 (Nov.) 1944.

Hypersensitivity: Ten drops of a solution containing 100,000 units per 5 ml. saline were placed on tongue every two hours and allowed to remain as long as possible before swallowing. After second day, soreness of tongue and throat, tenderness of gums, and marked injection of mouth and throat tissue developed. Kern, J. M. Soc. New Jersey, 42: 326 (Oct.) 1945.

Lung Instillation: 7.0 to 10 ml. in iodized oil was introduced into pulmonary lobe without adverse effect. Penicillin detected in urine after 24 hours. Romansky, Dugan, and Rittman, Science, 102: 255 (Sept. 7) 1945.

Oral Administration: 100,000 units dissolved in 8 ml. water plus 15 gm. aluminum hydroxide and kaolin and stirred for one minute, then water was added. Higher blood concentration was obtained with this method. Barach et al., Science, 102: 247; 1945.

Photosensitization: Urticaria of area exposed to sun developed within a day after 50,000 units were given. Canizares, Arch. Dermat. & Syph., 52: 17 (July) 1945.

Prolonging Action: 50,000 units in 2.0 to 2.5 ml. beeswax-peanut oil (0.75 to 6% beeswax suspended in peanut oil) maintained effective therapeutic titre for six to seven hours. Excretion in urine continued for 20 to 30 hours. Romansky, Bull. U. S. Army Med. Dept., 81: 43; 1944

Pruritus: Produced by 100,000 units given daily for ten doses, remained generalized for five days after discontinuance, then subsided gradually. Freyhan, Delaware State M. J., 16: 177 (Nov) 1944.

Sensitivity: Little antigenic potency. No patients developed sensitivity. Intracutaneously, extract of penicillin containing 0.01 or 0.1 mgm. nitrogen or solutions containing 200 to 10,000 units penicillin sodium were negative. No itching or edema. Grolnick and Loewe, J. Lab. & Clin. Med., 50: 559 (July) 1945.

Spinal Fluid. Present in 15 to 60 minutes after intramuscular injection of 10,000 to 20,000 units. Renal insufficiency raised blood and spinal fluid levels. Cook and Goldring, J.A.M.A., 127: 80; 1945.

Urticaria: Developed in rheumatic fever patients within 14 days. Average dose was 25,000 units of sodium salt intramuscularly at three hourly intervals for five days, a total of 1,000,000 units. Foster et al., J.A.M.A., 126: 281; 1944.

Vascular Collapse: Convulsions developed in a child following 50,000 units given intraventricularly after 100,000 units were given intramuscularly in six doses on previous day. 15,000 units, given intraventricularly, was tolerated later by same child (given eight times) Johnson and Walker, J.A.M.A., 127: 217; 1945

PENICILLIN SALTS

Mice--

Relative Toxicity: In increasing order: sodium, lithium, ammonium, strontium, calcium, magnesium, and potassium. LD₅₀ ranged from 43,036 units for the sodium salt to 7,956 units for the potassium salt. For pneumococcal infection, 50% protective dose varied from 437 to 525 units. Welch et al., J. Infect. Dis., 76: 52 (Jan-Feb) 1945.

PENICILLIN SODIUM

Staphylococci--

Inhibitory Effect: 0.01 mgm. per ml. of extracted organisms inactivated 800 units per ml. Spink and Ferris, Science, 102: 221 (Aug. 31) 1945.

Resistance: 0.1 mgm. dried bacteria from an osteomyelitis inactivated by 400 units per ml. Spink and Ferris, *Proc. Soc. Exper. Biol. & Med.*, 59: 188 (June) 1945.

PENICILLIN "X"

In Vitro—

Activity: Two to three times more penicillin "G" than penicillin "X" was necessary to inhibit 18 hour growth of types I, II, and III pneumococci; groups A, B, and D streptococci, *Erysipelothrix rhusiopathiae*, and *Escherichia coli*; on weight basis, 1.2 to two times more "G" than "X" was required. "X" inhibited *Esch. coli* in 46.875 units per mgm. concentration, and pneumococci types II and III in 0.005 unit per mgm. concentration. Libby and Holmberg, *Science*, 102: 303; 1945.

PENTAMIDINE

(See p. 85)

(4:4'-diamidino-diphenoxy pentane)

Guinea Pigs—

Prophylaxis: 0.002 gm/kg. three times gave 120 days protection against sleeping sickness. Van Hoof, Henrard, and Peel, *Tr. Roy. Soc. Trop. Med. & Hyg.*, 37: 271 (Feb.) 1944.

Man—

Prophylactic Use: Two, given single dose of 0.002 or 0.223 gm/kg. resisted repeated bites of tsetse flies for ten to 20 months. No sleeping sickness observed in Belgian Congo natives, given 0.002 to 0.003 gm/kg., intramuscularly. *Ibid.*

Therapeutic Use. Intramuscularly, 1.0 to 3 mgm/kg. was useful in early sleeping sickness. Intravenously, 1.0 to 2.0 mgm/kg. and/or intramuscularly, twice weekly had no benefit on advanced stage with central nervous system involvement. *Ibid.*

Trypanosomiasis: Intravenously, 0.5 mgm/kg. and gradually increased to 2.0 mgm/kg. improved 29 of 50 cases. Fall of blood pressure was only serious reaction, which was prevented by very slow injection. Saunders, Holden, and Hughes, *Ann. Trop. Med.*, 38: 159 (Dec.) 1944.

Leishmaniasis: Intramuscularly, 1.5 to 2.0 mgm/kg. three times a week for twelve to 15 injections cleared four of 11 patients. Temperature quickly fell to normal, but spleen was slowly reduced in size. Giraud and Revol, *Presse méd.*, 51: 291 (June) 1943; through *Trop. Dis. Bull.*, 41: 109 (Feb.) 1944.

PENTASTIB

(p-aminophenylstibinate of methyl glucamine)

Man—

Leishmaniasis: Intravenously, 20 to 200 mgm. for children under five and 50 to 300 mgm. for older children and adults, given three times a week for five weeks. Three courses were given. Drug resembled neotibosan in tolerance, but was less effective Giraud and Revol, *Presse méd.*, 51: 291 (June) 1943; through *Trop. Dis. Bull.*, 41: 109 (Feb.) 1944.

Visceral Leishmaniasis in Children: Recommended 0.07 gm/kg. intramuscularly for four days in three doses. Tested susceptibility with 0.25 gm. Sarrouy et al, *Texas Rep. Biol. Med.*, 2: 325; 1944.

PENTOBARBITAL, CALCIUM**Dogs—**

Dosages: Minimal effective dose was 25 to 30 mgm/kg. intravenously, and 20 to 25 mgm/kg. orally. Minimal lethal dose was 70 mgm/kg. intravenously, and 60 to 70 mgm/kg. orally. Drug was identical to sodium salt, pharmacologically. Scott and Livingstone, *Anesth. & Analg.*, 20: 350 (Nov.-Dec.) 1941.

PENTOBARBITAL SODIUM**Mice—**

Analeptic Activity: 65 mgm/kg. was given and 20 minutes later picrotoxin, amphetamine, leptazol, triazole, and methedrine were given intravenously. Goodwin and Marshall, *J. Pharmacol. & Exper. Therap.*, 84: 12 (May) 1945.

Rats (female)—

Duration of Sleep: Subcutaneously, 30 mgm/kg. caused longer sleep in normal than in castrate rats. Duration decreased with increased temperature of environment. Gaylord and Hodge, *Proc. Soc. Exper. Biol. & Med.*, 55: 46; 1944

Guinea Pigs, Rabbits, Cats, Dogs—

Uterine contraction and fetal behavior were not altered by 12 mgm/kg. Pankratz, *Am. J. Obst. & Gynec.*, 45: 877; 1941.

Rabbit Fetus—

Respiration: Intravenously, 5.0 or 10 mgm/kg. into maternal animal caused decrease in respiratory rate for less than 15 minutes, 20 mgm/kg. depressed fetal respiratory rate to one-third of initial level for half an hour; 30 mgm/kg. deeply depressed or abolished fetal respiration for

duration of experiment. Dreisbach and Snyder, *J. Pharmacol. & Exper. Therap.*, 79: 250 (Nov.) 1943.

Monkeys—

Denervated Muscle: Intravenously, 25 mgm/kg. caused contraction of denervated facial muscle in 11 of 12 animals, occurring 16 to 60 seconds after injection and lasting about 40 to 75 seconds. Bender, *Proc. Soc. Exper. Biol. & Med.*, 55: 146 (Feb.) 1914.

Man—

Poisoning: 3 gm. was ingested. Nikethamide intravenously, 1.5 ml. every 15 minutes for six doses, followed by six intramuscular injections of 1 ml. of metrazol every half hour plus gastric lavage and application of heat were ineffective. Picrotoxin, 21 mgm. injected intravenously in one hour elicited signs of awakening. Total amount of 135 mgm. was given. Patient fully recovered in two days, except for weakness. Billow, *J. Lab. & Clin. Med.*, 29: 265 (Mar.) 1914.

Basal Narcosis in Tonsillectomy: Elixir was most satisfactory. At least one hour before operation, child was given a dose equivalent of 0.05 gm. per 6.5 kg. Gerrie and Mackenzie, *Lancet*, 242: 759; 1912.

Obstetrics: 0.2 to 1.75 gm. produced respiratory complications in 35 of 10,097 cases; three patients died, one after 1.75 gm. and others after not more than 0.2 gm. Irving, *Rhode Island M. J.*, 28: 493 (July) 1915.

0.35 gm. had no effect on amplitude and interval of uterine contraction, diminished tonus. Bickers, *Virginia M. Monthly*, 69: 15 (Jan.) 1942.

Airsickness: 0.1 gm. plus 0.0013 gm. of atropine sulfate was given orally as prophylaxis, prior to takeoff to bomber crews. Green, *J. Aviation Med.*, 14: 366 (Dec.) 1943.

PENTOSE NUCLEOTIDE

Man—

Agranulocytosis and Aplastic Anemia: Unless marrow had become aplastic, improvements were obtained by early intensive treatment with pentnucleotide. 40 ml. was given daily for three days, then 10 ml. daily for two days. Ferguson, *Lancet*, 246: 334; 1944.

Infectious Mononucleosis. Granulocytopenia responded to intramuscular injection of 80 ml. given in three days (10 ml. three times daily on first day, 10 ml. twice a day on second day, and 15 ml. twice a day on third day). Sears, *Lancet*, 242: 703; 1942.

PENTOTHAL SODIUM

Guinea Pigs—

Dosages: Average lethal dose was 50 to 52.5 mgm/kg., intraperitoneally and minimum lethal dose was 37.5 mgm/kg., intraperitoneally for young animals. Average lethal dose was 55 mgm/kg. and minimum lethal dose was 40 mgm/kg., intraperitoneally, for adult animals Carmichael, Fed. Proc., 1: 13, 1942.

Rabbits—

Slough Prevention Subcutaneously, 5 ml. of 2.5, 5.0, and 10% solution produced skin reaction at site of injection, but those that received similar doses plus immediate infiltration of 5 ml. of 1% procaine hydrochloride in isotonic saline showed no tissue reaction. Elder and Harrison, J.A.M.A., 125: 116; 1944.

Rabbits (fetus at full term)—

Respiration: Intravenously, 10 mgm/kg. to maternal animal decreased respiratory rate to one-third initial level for five minutes, with 30 to 55 mgm/kg. total dose, little cumulative effect was noted Dresbach and Snyder, J. Pharmacol. & Exper. Therap., 79: 250 (Nov.) 1943.

Dogs—

Hemoglobin Concentration was 87 to 109% (average 94%) of pre-anesthetic concentration after 15 minutes of pentothal sodium anesthesia. Pender and Lundy, Anesthesiology, 5: 163 (Mar.) 1944.

Man—

Anesthesia. 1:250 to 1:1000 dilution in 5% glucose-saline solution intravenously for spinal or local for 512 patients, 1:500 dilution was satisfactory anesthetic for debilitated patients; and 1:1000 solution for sedation. Lenowitz, Lipson, and Stevens, Anesth. & Analg., 23: 78; 1944.

Intravenously, 10 ml. of 5%, first 5 ml. injected very slowly in two minutes. Patient usually asleep after 5 to 6 ml. Not satisfactory for tonsillectomy or esophagoscopy examination. Rachmel, Canad. M. A. J., 50: 443 (May) 1944.

Basal Narcosis: (pre-anesthetic) 0.5 gm. intravenously. Hudson, Current Researches in Anesth. & Analg., 23: 174 (July-Aug.) 1944.

Benefits and Hazards: Less than one gm. in healthy and robust or 0.5 to 0.75 gm. in weak, elderly or toxic patients. Adjuvant use of cyclopropane and nitrous oxide was more satisfactory. Deaths from obstruction of air passage. Subcutaneous injection caused local redness, swelling and tenderness in three and actual sloughing and healing in four to six weeks in five patients. Phlebitis in four resulted with intravenous injection.

Tenderness along vein with 10% solution; only 5% concentration should be used. Heard, *Anesthesiology*, 5: 448 (Sept.) 1944.

Cholecystectomies with continuous intravenous drip. 2.19 gm. was average dose for rectus block with procaine, and 1.23 gm. was average dose when splanchnic block was used. McCann, *New England J. Med.*, 233: 55 (July) 1945.

Cystoscopy: Intravenously, 2.5% in dosage of 2.5 to 42 ml. (average 11 ml.). Nesbit, *Bull. Am. Assoc. Nurse Anesthetists*, 10: 58 (May) 1942.

Death Rate: Six times higher in 7500 anesthetics than in any other. Safe procedure was routine administration of oxygen, careful observation of blood pressure and pulse, use of 2.5% solution, premedication with morphine, atropine 0.6 mgm. subcutaneously one hour before anesthesia, and 0.3 mgm. intravenously just before anesthesia. In emergencies, 0.6 mgm. of atropine was injected intravenously ten to 15 minutes before anesthesia. If laryngospasm occurred during operation, dose repeated intravenously as soon as possible. Contraindications were shock, morphine overdosage, neck infection, liver damage, and intracranial surgery. Poorly tolerated in severe burns. Bull. U. S. Army M. Dept., 76: 1 (May) 1944.

Dosage: A solution no stronger than 5%; dosage varied with individual, but in general, initial dose should be no more than three times amount required to induce sleep, and subsequent injection should be no larger than sleep dose. Smaller dose for patient in shock. Roberts, *Brit. M. J.*, 1: 825 (June) 1944.

Endoscopy: Intravenously, 2.5% solution subsequent to premedication with 10 mgm. morphine and 0.4 mgm. atropine given 45 minutes before surgery. Atropine omitted in patients with atelectasis. Spaid, *Anesth. & Analg.*, 23: 82; 1944.

Gravity Anesthesia: Gravity-feed apparatus for intravenous anesthesia eliminated risk of air or oxygen embolism, gave minute to minute control of effects of each dose, minimized blood pressure fall, and permitted anesthetist to administer oxygen, gas, and intravenous anesthetic simultaneously. 0.02 gm. pantopon and 0.4 mgm. scopolamine were given one hour before operation, 40 ml. 2.5% pentothal and 3 ml. nikethamide were administered alternately with physiologic saline. Griffin, *Brit. M. J.*, 1: 425 (Mar.) 1944.

Continuous intravenous anesthesia induced with 2.5% or 5% solution in a 20 ml. syringe connected with a gravity drip apparatus. A maintenance level was obtained with a 1% solution at an average rate of 20 drops a minute. Fierst, *M. Ann. District of Columbia*, 13: 50 (Feb.) 1944.

Hemoglobin Concentration: 81.3 to 100% (average 93.7%) in 15 men after 15 minutes of pentothal sodium anesthesia. Three men showed no decrease. Pender and Lundy, *Anesthesiology*, 5: 163 (Mar.) 1914.

Induction: No struggling upon induction of nitrous oxide + oxygen or ether anesthesia when patient was given 15 mgm. morphine plus 0.6 mgm. atropine one hour before operation, and 5% pentothal sodium. Dose was 1 ml. per second for 2 to 3 ml., then 1 to 2 ml. if respiration was greatly depressed; after 4 to 5 ml. was given, ear lobe was pinched, and if patient responded to this 1 to 2 ml. more was given. Brooks, *U. S. Nav. M. Bull.*, 42: 589 (Mar.) 1914.

Intrasternal Administration. Within one minute after an initial injection of 70 mgm., patient became drowsy. A total of 400 mgm. was given without complication except for postoperative drowsiness of four hours' duration. Lieberman, *New York State J. Med.*, 45: 2191 (Oct.) 1915.

Jaw Fractures: Intravenously, 0.25 to 0.5 gm. was given to 140 of 156 patients. Vomiting in 15 (9.6%); respiratory complications in 10 (6.4%); shock in 18 (11.5%), and two deaths. Shackleton, *Lancet*, 316: 396 (Mar.) 1914.

Neurologic Surgery: Excellent anesthesia in 378 intracranial operations. Average dose was 2.02 gm., average duration was 2.75 hours, and average time required for recovery from anesthesia was 4.5 hours. Woodhall and Goodman, *War Med.*, 4: 356 (Dec.) 1913.

War Neurosis: Intravenously, 0.25 to 0.4 gm. of 5% given two hours after meal before psychiatric interview. 33 of 50 rendered fit for duty. Drug was effective in hysteria and anxiety states, after-effects of head and spine injuries, borderline psychosis, mental deficiency and epilepsy when diagnosis was doubtful, and malingering. Wilde, *Brit. M. J.*, 11: 1 (July) 1912.

Ophthalmic Surgery: Apnea following use of pentothal sodium was treated with artificial respiration and intravenous injection of 0.13 to 0.26 ml. of 1:1000 epinephrine hydrochloride. Falls, *Arch. Ophth.*, 31: 131 (Feb.) 1914.

Obstetrical Anesthesia: Depressed respiration in mother and baby. 1.1 gm. produced 90 minute anesthesia for caesarean section, baby was stillborn. Brockman, *Bull. Am. A. Nurse Anesthetists*, 12: 13 (Feb.) 1914.

No maternal deaths or complications resulted in 101 patients given intravenously 175 to 1500 mgm. (average 625 mgm.) as 2.5% solution. Ruck, *Virginia M. Monthly*, 70: 35 (Jan.) 1913.

Safety Factors: Solution stronger than 2.5% was never used for intravenous anesthesia. Additional anesthetic after induction was given only

if patient started to move. Morphine and atropine premedication provided best results, also oxygen during anesthesia. Contraindicated in respiratory impediment. Marco, *Mil. Surgeon*, 95: 305 (Oct.) 1944.

Shock Therapy (modified): Intravenously, 300 mgm. in 2.5% solution in 30 seconds, followed by slow injection through same needle of 0.9 mgm. curare per kg. Current was applied four minutes after injection. Brody, *J. Nerv. & Ment. Dis.*, 102: 357 (Oct.) 1945.

Concentration in Body Fluids: (12 days after postpartum). Intravenously, 1125 mgm. was given and concentrations in mgm./100 ml. were determined. Oxalated blood, 20 minutes after injection started was 0.45; milk from left breast, 25 minutes after injection started, was 0.75; urine, 30 minutes after injection started, was 1.00; and milk from right breast, 14 minutes after injection was discontinued, was 2.00. Mayo and Schlike, *Proc. Staff Meet., Mayo Clin.*, 17: 87; 1942.

PEPTONE

Man—

Migraine: Desensitization with first dose of 0.25 ml. Dosage was then increased 0.25 ml. per dose at five day intervals to 2.0 ml. maximum. Mushin, *Lancet*, 242: 546; 1942.

PERCAINE

(2-butoxy-N-(β -diethylaminoethyl) cinchoninamide)

Man—

Caesarean Sections. Heavy solution of 1:200 with 6% glucose was used. Premedication with 0.6 mgm. atropine, 45 mgm. ephedrine, 45 minutes before operation. Area injected with 2% procaine, and required amount of percaine injected without aspirating cerebrospinal fluid. Thomas, *J. Obst. & Gynaec., Brit. Emp.*, 49: 247 (June) 1942.

PERTUSSIS

Mice—

Active Immunization. 5 ml. of standard, formalized, heat-killed pertussis vaccine, containing 10,000 million organisms per ml., was injected intraperitoneally. North, Anderson, and Graydon, *Med. J. Australia*, II: 589 (Nov.) 1941.

Phase I Vaccine. 0.3 to 0.4 ml. protected mice against a very large dose of living culture injected with mucin. Silverthorne and Cameron, *J. Pediat.*, 20: 1, 1942.

Man—

Protection of Contacts (in children): 5 to 10 ml. of immune rabbit serum was given intramuscularly. Silverthorne and Brown, J. Pediat., 20: 9; 1942.

Immunity Response in pregnant women: 0.5 ml., 1.0 ml., and 1.5 ml. of vaccine containing 10,000 million per ml. suspension of *Hemophilus pertussis* killed and preserved with 1:10,000 merthiolate, were given subcutaneously at weekly intervals. Pronounced rise in opsonins. Kendrick, Thompson, and Eldering, Am. J. Dis. Child., 70: 25 (July) 1945.

Treatment One to four 20 ml. doses intramuscularly, or a 40 ml. dose intravenously of hyperimmune pertussis serum were given to 23 critically ill children. Good results were obtained in 12, moderate in six patients. Paroxysms and cyanosis subsided in 24 to 72 hours after injection; after three to ten days clinical symptoms vanished. Scheinblum and Bullows, J. Pediat., 25: 49; 1944.

PERVITIN

(d-1)-(N-dimethylphenethylamine)

Rats—

Minimal Lethal Dose was 2.0 mgm/kg., subcutaneously. Blume and Zöllner, Arch. f. exper. Path. u. Pharmacol., 202: 21 (July) 1943.

Respiration: 0.05 and 0.1 mgm/kg., subcutaneously increased motility and 0.5 to 3.0 mgm/kg. increased both motility and respiration. Ibid.

Guinea Pigs—

Respiration: Very small doses (0.05 and 0.1 mgm/kg.) and very large doses (20.0 mgm/kg.) had an exciting effect and doses of 0.5 to 10.0 mgm/kg. a paralyzing effect on the respiratory volume. Ibid.

Minimal Lethal Dose was 10 mgm/kg., subcutaneously. Ibid.

Rabbits—

Hemostatic Action Intravenously, 100 gammas caused an average reduction in bleeding time of 68 seconds, 15 minutes later, and 72 seconds, one hour later. Derouaux, Arch. internat. de pharmacodyn. et de therap., 68: 311 (Dec.) 1942.

PHENANTHRIDIUM COMPOUND 897

(7-amino-9-[p-aminophenyl] 10-methylphenanthridinium chloride)

Cattle—

Trypanosoma congolense Infection: 11 of 40 animals were cleared with one dose of 2 mgm/kg., given subcutaneously, intramuscularly, and/or

intravenously. 22 of 27 relapses were cleared with 2 mgm/kg. intravenously. Highest nontoxic dose in eight was 3 mgm/kg. Carmichael and Bell, J. Comp. Path. & Therap., 54: 49 (Jan.) 1944; through Trop. Dis. Bull., 42: 259 (Apr.) 1945.

β -PHENETHYLAMINE

Guinea Pigs and Oxen—

Normal Blood Concentration was less than one part per million. Richter, Lee, and Hill, Biochem. J., 35: 1225; 1941.

Man—

Detoxication Rate: 26 mgm/kg. per hour after 75 mgm. was given intravenously. Ibid.

Normal Blood Concentration was less than one part per million. Ibid.

PHENOBARBITAL

Man—

Dermatitis: 0.1 gm. caused temperature rise and marked erythema over entire body which became pronounced on second administration. Anemia resulted after 0.1 gm. amytal and 0.22 gm. aminopyrine was given. Potter and Whiteacre, Ann. Int. Med., 21: 1041 (Dec.) 1944.

Poisoning: With 39 gm. in 19 year old male, after 1.5 gm. was taken nightly for some time. Recovered with 174 mgm. picROTOXIN in four days. McNally and Horwitz, Illinois M. J., 86: 317 (Dec.) 1944.

Poisoning and Death: Cutaneous eruptions and death from 1.26 to 5.5 gm. taken over a two to three weeks period. Sexton, Pike, and Nielson, J.A.M.A., 116: 700; 1941.

Rash: 0.06 to 0.12 gm. daily for eight to 12 days given to children, caused sudden decrease in number of paroxysms and coincidental termination of pertussis directly after appearance of morbilliform rash which disappeared in three days after withdrawal of drug. Vollmer, Urol. & Cutan. Rev., 48: 88 (Feb.) 1944.

PHENOBARBITONE SOLUBLE

Guinea Pigs—

Effect on Cholinesterase. Subcutaneously, 10 to 16 mgm. three times a day for 14 to 18 days reduced cholinesterase activity of muscle and spinal cord extracts of guinea pig serum approximately 40% and 50%, respectively. Subcutaneously, single dose of 60 mgm. did not affect cholinesterase of brain, spinal cord, and serum within three hours. Schütz, J. Physiol., 102: 269 (Dec.) 1943.

Single, subcutaneous dose of 40 mgm. had no effect on cholinesterase activity of serum. Schütz, J. Physiol., 102: 259 (Dec.) 1943.

Man—

Effect on Cholinesterase: Single oral dose of 195 mgm. had no effect on cholinesterase activity of the serum, two, eight, and 24 hours after dose had been given. It was estimated that there was 22% reduction in enzyme by prolonged administration of drug. Ibid.

PHENOL

Chick Embryos—

Smallest amount causing death was 0.05 gm/kg. Dunham, Proc. Soc. Exper. Biol. & Med., 50: 274 (June) 1942.

Rabbits—

Distribution and Excretion: Animals killed one to three minutes after oral lethal dose (0.5 gm/kg.). Drug was found in largest amounts in liver, central nervous system, lungs, and blood, and detoxication by conjugation had started. Animals killed 24 hours after administration of 0.3 gm.: 3% was present in carcass, 20% destroyed, 77% excreted in urine, and traces in feces and exhaled air. Animals living 15 minutes to six hours after oral lethal dose had almost complete anuria, 50% was destroyed in two and a half to six hours and other 50% was recovered from carcass. After two and a half hours, recovered phenol was in free form, after six hours in conjugated form. Deichmann, Arch. Biochem., 3: 345 (Feb) 1944.

Man—

Lethal Dose Smallest dose causing death was 0.07 to 0.14 gm/kg. Dunham, Proc. Soc. Exper. Biol. & Med., 50: 274 (June) 1942.

Poisoning Local use of mixture of 31 gm. camphor plus 125 gm. phenol resulted in death in 15 minutes from acute pulmonary edema. Stomach, spleen, heart, and kidneys revealed phenol. Miller, Canad. M. A. J., 46: 615 (June) 1942.

PHENYLALANINE (FLUORINATED)

Rats—

LD₅₀ 20 mgm/kg for 3-fluorophenylalanine. Boyer, Evans, and Phillips, J. Pharmacol. & Exper. Therap., 73: 176; 1941.

PHENYLAMINOPROPANE

Man—

Opposing Action Inhalation for ten to 15 minutes in a mist chamber into which a 5% solution of drug was nebulized caused hypoventilation,

and inhalation for 50 to 60 minutes reversed the phenomenon, resulting in hyperventilation, with tachypnea. Dautrebande et al., Arch. internat. de pharmacodyn. et de therap., 68: 247 (Dec.) 1912.

Respiratory Effect: Ingestion of 5 to 30 mgm. gave rise to hypopnea, bradypnea, and an increase in volume of each inspiration within ten minutes. Pulmonary ventilation decreased from 301 to 273 liters, while volume of each inspiration increased from 696 to 1220 ml. Dautrebande et al., Arch. internat. de pharmacodyn. et de therap., 68: 451 (Dec.) 1942.

PHENYL CELLUSOLVE

Man (children)—

Pediculosis Capitis: One application of 5%, 10% or 20% lotion completely eradicated living lice and nits from 25 cases. No toxicity. Hansens, Am. J. Hyg., 41: 5 (Jan.) 1915.

One part phenyl cellusolve, two parts ethanol, two parts water, and methyl salicylate (for odor) controlled lice. Davis, Juvera, and Lira, Am. J. Hyg., 39: 177 (Mar.) 1944.

PHENYLHYDROXYLAMINE

Cats—

Methemoglobin: Subcutaneously, 0.5 mgm/kg. converted 50% of blood pigment to methemoglobin, reaching maximum in one hour. 0.5 mgm/kg. daily for five to nine weeks caused same degree of anemia as on second day after single injection of 5 mgm. m-dinitrobenzene per kg. Schlime, Arch. f. exper. Path. u. Pharmacol., 202: 60 (July) 1913.

PHENYL PHENOLS

Mice—

Inhalation. Air saturated with diphenyl or o-phenyl phenol vapor showed no harmful effects. Macintosh, Analyst, 70: 334 (Sept.) 1945.

Rats—

Minimal Lethal Dose: was 3 gm. of o-phenyl phenol per kg.; and 1.5 gm. and 0.5 gm. of o-phenyl phenol per kg. respectively, in nut oil and in gum acacia suspension. Ibid.

Repeated Administration: Orally, 2 to 200 mgm diphenyl per kg. o-phenyl phenol for four weeks or 32 days, respectively, affected blood forming tissues. Hemoglobin content, total white cell count, and differential white cell count were not altered. Ibid.

Rabbits—

Toxicity: Subcutaneously, 0.5 ml. of a 4% diphenyl solution into the rabbit's ear, and intraperitoneally, 0.5 gm. per kg. were non-toxic. Ibid.

Cats—

Toxicity Tolerated up to 1.0 gm/kg. orally, of diphenyl phenol. MLD: 0.5 gm/kg. of o-phenyl phenol per kg. Hemorrhage in the lungs, liver, alimentary canal, and myocardium were seen at autopsy. Ibid.

Man—

Inunction: 0.5 ml of a 4% diphenyl solution rubbed into forearm skin was nontoxic. Ibid.

PHENYL-PROPYL-METHYLAMINE HYDROCHLORIDE

(Vonedrin)

Man—

Asthma Symptomatic improvement of six of ten patients, aged nine to 81, given 25 mgm. orally, four to eight times a day for five to six months. Blood pressure remained constant in seven and decreased in three; in eight of ten weight was constant. No central nervous system stimulation, mydriasis, tremor, insomnia, nervousness, etc. Glacer, Clin. Med, 51: 63 (Mar.) 1944.

PHENOTHIAZINE**Anopheles Larvae—**

Control All disappeared in 48 hours when 200 and 400 gm. were used per acre. Contact for one to one and a half hours killed larvae in laboratory tests. Nesterwodskaia and Lubinski, Deut. Trop. Z., 47: 252 (May) 1943; through Trop Dis Bull, 41: 102 (Feb) 1944.

Aquarium Fish—

Toxicity 1 mgm/100 square cm. killed 10% of fish in four days. Ibid.

Sheep—

Therapy of Parasites (*O. columbianum*, *B. trogonoccephalum*, *H. contortus*). 25 gm at two weeks' intervals Hay, J. Am. Vet. M. A., 98: 462; 1941.

Repeated Doses were given to nine yearling lambs. Single 25 mgm dose or six weekly 25 mgm doses had no effect on hemoglobin level or weight gains. Wright, Vet. Med, 37: 33 (Jan.) 1942.

Parasitic Gastritis in Lambs was treated with free access to 1.100 phenothiazine-salt mixture Britton, Vet Med., 39: 239 (June) 1944.

Cattle—

Anthelmintic Three month calves to adult cattle were treated with 30 to 80 gm., depending on size, after fasting for 18 to 24 hours. Swanson and Carlisle, Vet Med, 36: 312, 1941.

Horn Fly Control Effective dose was 1 gm per cwt, but imparted

reddish tinge to milk. 2.25 gm. or more per cwt. caused loss of appetite, gaunt appearance, dullness of eyes, and nervousness. Bruce, J. Kansas Entomol. Soc., 13: 41; 1911; through Exper. Sta. Rec., 84: 222; 1941.

Parasitic Gastritis: 12 to 15 gm. for calves, and 20 to 30 gm. for yearlings. Britton, Vet. Med., 39: 239 (June) 1944.

Stomach and Nodular Worms in calves removed with 0.4 gm/kg. Simms, Proc. Assoc. Southern Agr. Workers, 42: 250; 1941.

Toxicity to Calves: Single and multiple doses of 8 to 100 mgm. were non-toxic. 20 gm. per cwt. to a maximum of 60 gm. was non-toxic. Cauthern, J. Am. Vet. M. A., 107: 71 (Aug.) 1945.

Horses—

Anthelmintic: Minimal effective dose was 30 gm. for mature thoroughbreds and 45 gm. for largest thoroughbreds. Albuminuria resulted in previously medicated pregnant and yearling animals given 30 and 15 gm., respectively. Errington, Vet. Med., 36: 188 (Apr.) 1941.

Effect of Large Doses: Four horses were given by stomach tube 324 gm., 80 gm., 160 gm., and 400 gm., respectively. First horse died; second showed no effect; anemia in others. Boley, Morrill, and Levine, Vet. Med., 37: 26 (Jan.) 1942.

Strongylosis: Treated with 20 to 30 gm. in divided doses for 450 kg. horse. North Am. Veterinarian, 24: 721 (Dec.) 1943.

Four weeks' treatment with 40 gm. decreased ova in feces. Rosoff, North Am. Veterinarian, 24: 737 (Dec.) 1943.

Animals—

Lung Worms: Intratracheally, 30 gm. in 100 ml. of a mixture of equal parts of glycerol and alcohol killed lung worms. Dosages: chickens, 0.1 to 0.5 ml.; lambs, 2 ml.; ewes, 3 to 9 ml.; rams, 10 to 12 ml.; goats, 5 ml. Contraindication of intratracheal injection for sheep and goats with advanced pneumonia or caseous lymphadenitis. Eveleth, Eveleth, and Gifford, Vet. Med., 38: 63 (Feb.) 1943.

Man—

Intestinal Helminthic Infestations: Treated with 2 gm. three times a day for a total dose of 20 to 30 gm. over four to five days in West African natives. American standard of 1 gm/4.5 kg. was safe since no intolerance was experienced with twice the dose. Elliott, Tr. Roy. Soc. Trop. Med. & Hyg., 37: 163 (Sept.) 1943; through J.A.M.A., 124: 326; 1944.

Fatality in Child: 8.5 gm. in five days produced jaundice, hemolytic anemia, and death. Lancet, 1. 86; 1942.

Pinworm Therapy: Orally, 2 gm. for adults and 0.25 to 0.5 gm. for

children under two, daily for seven days. This course was repeated after one week. Sisk, North Carolina M. J., 5: 52 (Feb.) 1944.

Pinworm Therapy in Children Total dose of 7 gm. in three days was 100% effective. Miller and Allen, Canad. M. A. J., 46: 111 (Feb.) 1942.

Threadworm Remedy in Children. 1 gm/kg. was given in three to five days. Second course was given after one week of rest, if necessary. Hubble, Lancet, 241: 600; 1941.

PHENYL MERCURIC NITRATE

(Merphenyl nitrate, basic)

Rabbits—

MLD Intravenously, 7 ml/kg of an 0.067% (1:1,500) aqueous solution of basic salt buffered with 1% boric acid. Orally, dose was approximately three times intravenous. J.A.M.A., 117: 1784; 1941.

PHENYLTHIOCARBAMIDE

Rats—

Graying. Gradually increased concentration of 0.001% to 0.1% in drinking water caused graying of hair in 58 days. Color returned in 83 days after withdrawal of drug. Richter and Clisby, Proc. Soc. Exper. Biol. & Med., 48: 684 (Dec.) 1941.

Toxicity: Orally or by injection, 1.0 to 10.0 mgm caused death in two to 18 hours with marked respiratory distress and decrease in body temperature. Median lethal dose was near 10 mgm. Progressively larger doses administered over 20 to 80 days increased tolerance to 12 mgm. per day. Richter and Clisby, Arch. Path., 33: 46 (Jan.) 1942.

PHLORIZIN

Man—

Liver Glycogen Two intravenous injections of 1 gm. in 0.1 N sodium hydroxide was given at three hour intervals. Fall of blood sugar level from immediately before to six hours after first phlorizin injection was inverse measure of adequacy of liver glycogen. Diabetic adults, normal and diabetic children, and patients with liver dysfunction showed lower liver glycogen reserve, therefore greater susceptibility to ketosis. Karenberg, Arch. Int. Med., 72: 746 (Dec.) 1943.

PHOSGENE

Man—

Poisoning Acute case was treated by placing patient in oxygen tent, giving sedation and 50% glucose intravenously, and 1 gm. sulfadiazine

every six hours to a total of 15 gm. to prevent secondary pneumonia. Generalized râles disappeared by tenth day. Sage, Am. J. Roentgenol., 51: 9 (Jan.) 1944.

PHOSPHATE, SODIUM ACID

Man—

Flatulence: 1 gm. three times a day brought marked improvement to 13 patients. McDowell, Lancet, 246: 294; 1944.

PHOSPHORUS

Reptiles and Birds—

Blood Content: Birds' blood contained 90 to 135 mgm/100 ml. with high proportion of phytic acid. Reptile blood was variable; turtle had phytic acid and snake had adenosine triphosphate. Rapaport and Guest, J. Biol. Chem., 138: 269; 1941.

Cows, Sheep, Goats, Deer—

Blood Phosphorus: 9 to 15 mgm/100 ml. and traces of phosphoglycerate. Ibid.

Mammals—

Blood Phosphorus: Mammalian blood contained 50 to 100 mgm. of organic acid-soluble phosphorus in 100 ml. in form of phosphoglycerate. Ibid.

Poisoning: 130 mgm. in rat paste was taken orally; recovery. Gastric lavage, copper sulfate (0.25 gm.), potassium permanganate (1:1000), or 2% hydrogen peroxide, and magnesium sulfate cathartic recommended. Cretien, New England J. Med., 232: 247 (Mar.) 1945.

PHOSPHORUS, RADIOACTIVE

Radioactivity Assay—

Method: Fractions of blood, and aliquot portions of feces and urine were ashed at 400° C. and radioactivity of each ash was measured by the Du Bridge electrometers, Lauritsen type of electroscopes or Geiger counters, each of which was standardized to emit 500 beta particles per second. Erf, Tuttle, and Lawrence, Ann Int. Med., 15: 487 (Sept.) 1941.

Mice—

Lethal Dose: That amount given intraperitoneally to a 20 gm. mouse, which emits 70 micro-curies of beta-radiation. Ibid.

Monkeys—

Lethal Dose. Intraperitoneally, seven milli-curies for a six pound monkey. Ibid.

Man—

Excretion: 26.1 to 50.5% of dose was excreted during six days after intravenous administration by normal individuals; 5.6 to 24.5% during four to six days by myeloid leukemia patients; and 2.79 to 16.5% by those with lymphoid leukemia. 22.9 to 46.3% of the dose was excreted in urine and feces during six days following oral administration; 14.1 to 45.5% during four to six days by myeloid leukemia patients, and 37.8 to 53.9% by lymphoid leukemic patients. *Ibid.*

Lethal Dose (suggested): Well over 100 milli-curies. *Ibid.*

Leukemia: Single oral doses varied from one to 20 milli-curies and single intravenous doses varied from 0.5 to 0.6 milli-curies depending on age and type of disease. Half-life was 14.3 days, so there was no danger of cumulative radiation. Regardless of chronicity or acuteness of leukemic process, P^{32} levels of white blood cells rose during first 48 hours and then continued to rise or maintained high plateau for days. Two cases showed complete remission for two years. *Ibid.*

Polycythemia Vera. Intravenously, initial dose was 4 to 7 mc. (milli-curies) of P^{32} , total dose ranged from 2.02 to 15.68 mc. P^{32} in 12 patients. Complete remission was obtained in eight and partial in two. Hall et al., *Am. J. M. Sc.*, 209: 712 (June) 1945.

Therapeutic Use: Temporary relief was obtained in 27 of 81 cases with leukemia, myeloma, Hodgkin's disease, and polycythemia vera. P^{32} was administered as Na_2HPO_4 , $MgNH_4PO_4$, and H_3PO_4 . Dosage was individual; desired dose for adults was given intravenously in 300 ml. of 0.85% sodium chloride and 5% glucose; and for children and infants in 100 ml. Orally, 150 ml. orange juice was diluent, but intravenous route was preferable as 20 to 30% of oral dose was lost by precipitation in gastro-intestinal tract. Warren, *Am. J. M. Sc.*, 209: 701 (June) 1945.

Toxicity: Intravenously, radioactive phosphorus in form of magnesium ammonium phosphate and of phosphoric acid dissolved in 0.85% sodium chloride and 5% glucose were harmless to experimental animals or man. Amounts injected were 1,100 to 3,900 and 1,000 to 4,000 micro-curies, respectively. Warren and Cowing, *Cancer Research*, 4: 113 (Feb) 1944.

PHTHALIC ACID AND DERIVATIVES

Mice—

Toxicity: LD_{50} was 0.55 gm/kg. intraperitoneally of phthalic acid. Cyanosis and spasmodic movements. LD_{50} for di-n-butyl phthalate was 5.5 ml/kg. LD_{50} for di-octanol-2, phthalate was 46 ml/kg. Hodge et al., *Proc. Soc. Exper. Biol. & Med.*, 49: 471 (Mar.) 1942.

PHYSOSTIGMINE SULFATE

Man—

Vomiting in Pregnancy: Orally, if possible hypodermically, 0.00065 gm. twice a day or three times a day. 29 of 31 recovered. Two pilots also responded after persistent morning vomiting. Turnbull, South African M. J., 17: 279 (Sept.) 1943; through J.A.M.A., 124: 326; 1944.

PHYTONCIDES

Protozoa—

Toxicity: Unicellular organisms were killed within one to five minutes by small amounts of freshly macerated onion, garlic, or other allium paste. Tokin, Compt. rend. acad. d. sc., U.S.S.R., 38: 215; 1943; Am. Rev. Soviet Med., 1: 237 (Feb.) 1944.

Rabbits—

Inhalation: Exposure to vapor from freshly prepared onion paste for four minutes ten times a day for ten days caused pronounced stimulation of wandering cells of connective tissue and slight reversible changes in parenchymatous organs in animals sacrificed one, five, and 15 days after last inhalation. Toroptsev, Compt. rend. acad. sc., U.S.S.R., 38: 254; 1943; through Am. Rev. Soviet Med., 1: 242 (Feb.) 1944.

Wound Therapy: Exposure of experimentally infected wounds to onion paste vapors, ten to 15 minutes a day, caused rapid healing, whereas control wounds in same animals showed progressive inflammation and necrosis. Toroptsev and Filatova, Khirurgia, 5-6: 15; 1943; through Am. Rev. Soviet Med., 1: 244 (Feb.) 1944.

Purulent Wounds: Amputation stumps exposed to onion paste vapors for ten minutes daily brought relief from pain and a marked acceleration of regenerative processes. Ibid.

PICROTOXIN

Man—

Barbiturate Antidote: Intravenously, 1 ml. per minute of a solution containing 3 mgm/ml. was given until movement appeared in lips, eyelids, and extremities. Then rate was 1 ml. per five minutes to keep patient at minimal motor activity, then gradually reduced from 1 ml. per 10 minutes to 1 ml. per 15 minutes and finally discontinued when patient responded to external stimuli. Percy and La Due, South. M. J., 38: 726 (Nov.) 1945.

2.0 ml. antidoted 10 ml. pentothal sodium within 15 minutes. Murphy, Brit. M. J., II: 93 (July) 1944.

Intravenously, 27 mgm. in 0.3% (isotonic) aqueous solution prevented

death from 1.46 gm. nembutal poisoning. Fishman, *Lancet*, 242: 199; 1942.

Intravenously, continuous drip at rate of 1 ml. (3 mgm.) per minute was given until twitchings occurred, after which dose was decreased. 1 ml. every five minutes was then required. Intervals between doses were increased to ten and then to 15 minutes, and drug was discontinued when patient responded to minimal stimulation. Cases of 1.2 gm. secenal and 0.8 gm. nembutal overdosages responded to total doses of 321 and 307.5 mgm., respectively. Dorsey, *J. Nerv. & Ment. Dis.*, 99: 367 (Apr.) 1944.

Time Factor as Antidote: 42 hours after 4.25 gm. pentobarbital sodium was taken, 0.238 gm. of picrotoxin was given over a 36 hour period; recovery with blurred vision, tingling of hands and feet, sluggish memory. Complete recovery when treatment was started 12 hours after 9 gm. pentobarbital sodium was ingested with 0.003 gm. picrotoxin per minute intravenously, and obtained response in 40 minutes. Treatment was continued with 0.003 gm. per 15 to 30 minutes, intramuscularly, for five hours and discontinued after 0.192 gm. was given Burdick and Rovenstine, *Ann. Int. Med.*, 22: 819 (June) 1915.

Recommended Dosage as Antidote: 0.001 to 0.003 gm. intravenously, or 0.003 to 0.006 gm. intramuscularly, every 15 minutes until desired response is obtained. Intravenous route should be discarded if twitching appears. Supportive measures are establishment of adequate airway, artificial respiration, administration of oxygen, gastric lavage, chemotherapy, and diuretic stimulation. *Ibid.*

Antidote: 174 mgm. given in four days promoted complete recovery from phenobarbital poisoning with 39 gm. of hypnotic. P. Chauchard et al., *Compt. rend.*, 217: 619, 1943.

PILOCARPINE

Dogs—

Effect. Subcutaneously, doses of 0.01 to 1.0 mgm/kg. into stomach pouch of dogs did not directly stimulate mucus secretion at neuroglandular junction. 0.5 to 1.0 mgm/kg. caused defecation, restlessness, salivation, mucosal bleeding, and vomiting. Hollander and Stein, *Am. J. Physiol.*, 140: 136 (Nov.) 1943.

Man—

Sweat. Injection of 0.016 gm. resulted in almost complete anhidrosis below the neck and hyperhidrosis above in eight soldiers with syndrome of sweat mechanism failure. Wolkin, Goodman and Kelley, *J.A.M.A.*, 124: 478; 1941.

PITOCIN

Man—

Blood Pressure: Intravenously, ten units in three unit doses or injection into uterine wall of non-pregnant and three to six months pregnant, and intravenous injections in males caused decreased arterial blood pressure of 30 to 50 mm. of mercury for two to five minutes. Woodbury et al., J. Pharmacol. & Exper. Therap., 81: 95 (May) 1944.

Effect on Pregnancy: Subcutaneously, 0.66 oxytocic unit or 0.05 mgm. sublingually increased uterine activity without producing any fusion or contractions. Woodbury et al., J. Pharmacol. & Exper. Therap., 80: 256 (Mar.) 1944.

PITRESSIN

Rats—

Antidiuretic Action: Effect of 0.02 milli-unit or 20 micro-units given intravenously could be detected in single rats rendered diuretic by administration of water and alcohol in sedative dosage. Test was ten times more sensitive than using rabbit. (Walker, Am J. Physiol., 127: 519; 1939) or multiple rat test (Burn, Quart. J. Pharm. & Pharmacol., 4: 517; 1931). Jeffers et al., Proc. Soc. Exper. Biol. & Med., 50: 184 (May) 1942.

Cats—

Repeated Administration: 0.1 to 3.0 ml. intravenously or intramuscularly, given in two to 19 doses, produced changes in myocardium, electrocardiogram, and cerebral cortex resembling those produced by toxic doses of digitalis. Dearing, Barnes, and Essex, Am. Heart J., 27: 96 (Jan.) 1944.

Dogs—

Renal Effect: 0.3 to 0.6 units per kg., given subcutaneously or intramuscularly, produced variable but slight changes. Intravenous injections caused transient anuria followed by oliguria for several minutes and marked decrease in renal blood flow. Sudden and transient rise in blood pressure resulted with intravenous injections, followed occasionally by a transient fall and then a gradual, prolonged but moderate rise lasting for 15 minutes. Wakim et al., J. Lab. & Clin. Med., 27: 1013 (May) 1942.

Man—

Abdominal Surgery: Five to ten units or 0.5 ml. was injected intramuscularly one-half hour before operation. Postoperatively, 0.5 ml. was administered within four hours and continued at six hour intervals for four doses. Good results, no gas pains for 48 hours and less morphine required to relieve pain. Contraindicated in intestinal obstruction, cardiorenal disease, hypertension, advanced arteriosclerosis, and coronary

thrombosis. Wylie, J. Florida M. A., 28: 229 (Nov.) 1911.

Diabetes Insipidus: Intramuscularly, 0.5 ml. of pitressin solution (1.0 ml. \approx 20 international units) per day controlled diabetes insipidus in boy, Wylie, Proc. Roy. Soc. Med., 36: 581 (Sept.) 1943.

Hemostatic in transurethral resection. 0.9 ml. of pitressin plus 0.3 ml. epinephrine diluted to 15 ml with distilled water; 6 ml. was injected into prostatic capsule at close of operation Emmett and Lopez-Engelking, Proc. Staff Meet., Mayo Clin., 18: 525 (Dec.) 1913.

Idiopathic Epilepsy (diagnosis) Subcutaneously, 0.25 ml., followed by 0.5 ml. at four hour intervals for ten doses or until
400 ml. of water

at two hour intervals. (Frederick, 1912.)

Oliguresis. During penicillin therapy a transient oliguresis occurred in 1 patient, who was treated for 24 days. (J. A. M. A., 128, 1161; 1915.)

PITRESSIN TANNATE

Man—

Diabetes Insipidus. Treatment with 1-2 . . . : . ,
which suggests
seven
days

Intramuscularly, 0.25 ml in oil (1 ml. = 5 international units) per day gave better response than pitressin in four boys. *Wyllie, Proc. Roy. Soc. Med.*, 36: 581 (Sept.) 1943

PITUITARY

Xenopus Laevis—

Assay—Maximum melanophore index was criterion of potency (10% accurate) attained after injection into dorsal lymph sacs of fully pale, intact or hypophysectomized animals. Landgrube and Waring, Quart. J. Exper. Physiol., 33: 1 (Sept.) 1911.

PITUITRIN

Mag-

Cæsarean Operation. Two ampules injected into anterior wall of uterus immediately after extraction of fetus hastened conclusion of operation with immediate contraction of uterus, facilitating separation of placenta, and greatly reducing hemorrhage. Rubenito Bol do Saui.

São Lucas, 3: 179; 1942; through Am. J. Obst. & Gynec., 47: 132 (Jan.) 1944.

Renal Tubular Function Test: 0.5 ml. (ten units) of surgical pituitrin was injected subcutaneously after voiding, and then specific gravity of urine specimens collected at half hour intervals during next two hours was determined. Impairment of renal tubular function was characterized by impaired concentrating ability reflected in specific gravity. Engelhardt, Am. J. M. Sc., 203: 812 (June) 1942.

PLASMA

Bacteria—

Contamination Prevention: Blood was drawn directly into solution containing 1.5 gm. sodium citrate and 1 gm. sodium sulfathiazole sesquihydrate in 50 ml. physiologic saline. Novak, J.A.M.A., 118: 513; 1942.

Dogs—

Blood Substitute. Dogs bled maximum amount from carotid replaced by equal amount of plasma with 20 mgm. heparin per liter caused 6% deaths, while all other blood substitutes produced higher mortality rates. Ivy et al., Surg., Gynec. & Obst., 76: 85 (Jan.) 1943.

Shock Therapy: Concentrated plasma injected into femoral vein at rate of 50 ml. in one to five minutes' time produced rapid hemodilution in animals in post-hemorrhagic and traumatic shock. Muirhead, Ashworth, and Hill, Surgery, 12: 14 (July) 1942.

Man—

Burn Therapy: In early transfusion, 500 ml. plasma was given for each 10% of body surface burned, but if shock was already imminent, 100 ml. plasma for each per cent that the hematocrit was above 45 was given. Cope, J.A.M.A., 125: 536; 1944; and 125: 731; 1944.

Cadaver Plasma: Dried plasma and serum obtained eight hours after sudden death restored to 25% original volume with distilled water was given intravenously to patient with teratoma. Patient died six or seven weeks after last administration with no changes related to plasma on microscopic study of organs Erf, Am. J. M. Sc., 207: 314 (Mar.) 1944.

Epidemic Meningitis: Six of seven recovered with intravenous administration of blood plasma containing 2 to 5% sodium salts of sulfapyridine or sulfathiazole, in 15 to 20 minutes, with repetition as needed. Vargas Baeza, Rev. de med y alimentacion, 5: 292; 1943; through Quart. Rev. Med., 1: 89 (Feb.) 1944.

Gastro-enteritis. Infants improved following one or more intraperi-

toneal injection of 75 to 150 ml blood plasma. Curtin, Pennsylvania M. J., 47: 575 (Mar.) 1944.

Infectious Mononucleosis: 500 ml. was given intravenously. Death occurred. Autopsy showed hepatitis, nephritis, splenitis, and pneumonitis of a peculiar type. Ziegler, Arch. Path., 37: 196 (Mar.) 1944.

Osmotic Activity. Total osmotic activity of serum or heparinized plasma of 28 normal men (20 to 35) was 152 to 159 (mean, 155.5, standard deviation: 1.9) milli-equivalent sodium chloride per kg. water at 37.5° C. in a gas phase of 5% carbon dioxide in oxygen. Lifson, J. Biol. Chem., 152: 659 (Mar.) 1944.

Polioomyelitis: 1.25 liters followed by 1 liter the same day. Patient became rational in 24 hours, received two doses of 500 ml., and returned to duty few weeks later. Spectacular response in seven others. Barnum and Bower, U. S. Nav. M. Bull., 42: 730 (Mar.) 1944.

Venopressor Effect. Marked increase in intramuscular pressure followed by an increase in venous pressure occurred in seven patients receiving three units of plasma, while no change occurred in one patient receiving one unit of plasma. Gunther and Meeker, Am. J. Physiol., 141: 102 (Mar.) 1944.

War Wounds and Burns. In severe burns, the first 1.5 liters was given at rate of 0.5 liter per 5 minutes with use of pressure. Four to 12 liters were often needed in first 48 hours, and as many as 15 liters in first five days. Rankin et al., Clinics, 2: 1194 (Feb.) 1944.

PLASMA, LYOPHILE

Man--

Infant Diarrhea Therapy. Subcutaneously, 50 ml. of pooled lyophile plasma was followed by 25 ml. daily for four days, and 0.4 gm. sulfathiazole powder in three bottle feedings. Prophylactic therapy consisted of 25 ml. daily plus 0.2 gm. sulfathiazole three times daily. Arch. Pediat., 58: 751 (Dec.) 1941.

Hemophilia Management. 125 ml. weekly injections for three months were given to totally disabled case with coagulation time of 100 minutes. Coagulation time fell to normal during first 24 hours after injection, reaching 60 minutes at end of six days. Patient was hemorrhage free during treatment. J. A. M. A., 118: 799, 1942.

Uses: 200 ml., given during first 24 hours, treated a case of hematuria. 150 ml. reduced coagulation time to normal, permitting tooth extractions of hemophiliacs. Ibid.

PLASMODIUM LOPHURAE**Ducks—**

Malaria Immunization: A total of 37 billion killed parasites, given in three monthly injections, developed resistance to infection with approximately one billion *P. lophuræ* parasites. Freund, Sommer, and Walter, Science, 102: 200; 1915.

PLATYPHYLLIN**Man—**

Antispasmodic: Alkaloid from *Senecio platyphyllus* was well tolerated hypodermically, orally, or by suppository. Had no disagreeable side effects of atropine. Antispasmodic action was superior to atropine in gastric ulcer. 0.6 to 1.0 ml. orally, three times a day; hypodermically only in severe pain; 1.0 to 2.0 ml. 1:500 solution subcutaneously in mild colitis and gastritis. Acute pain subsided in ten to 15 minutes. Goldhershel, Klin. med., 31: 56; 1943; through Am. Rev. Soviet Med., 1: 155 (Dec.) 1913.

ANTIPNEUMOCOCCUS SERUM**Man—**

Dose: Intravenously, 20,000 to 100,000 units of Type IV from rabbits. Council on Pharm. & Chem., J.A.M.A., 117: 1264; 1941.

Pneumonia: If there was no response to chemotherapy in 24 to 36 hours, a specific antipneumococcus serum, an initial dose of 100,000 units and added doses of 50,000 to 100,000 units within six to eight hours, was indicated. Initial dose was doubled in patients over 40 years, where treatment had been commenced later than third day, when a positive blood culture was present, or when two or more lobes were involved. When combined with sulfanilamide, an initial dose of 50,000 to 75,000 units repeated in six to ten hours, was usually sufficient. McCreary, Pennsylvania M. J., 47: 493 (Feb.) 1944.

POISON IVY**Man—**

Dermatitis Venenata: 5% alcoholic extract of poison ivy leaves was used in 1851 patients. Average number of injections was four per patient. Marked itching, burning, and smarting were alleviated by first and second injections; and duration of lesion was shortened. Good results obtained in 68% and fairly satisfactory results in 18.4%. French and Halpin, Ann. Allergy, 1: 131 (Sept.-Oct.) 1943.

Prophylaxis: 0.2 ml. of 1:100 dilution of alcoholic extract was given

subcutaneously, and gradually increased until top dosage of 0.5 ml. of 1:10 dilution was reached after eight injections at twice weekly intervals. Ibid. Orally, 0.25 to 0.5 mgm. oleoresin daily, increased according to tolerance up to 10.0 mgm. Total dose was 1,196.75 to 3,357.25 mgm. per person. Gold and Masucci, *J. Allergy*, 13: 157 (Jan.) 1942. Two drops to 25 ml. of oleoresin in corn oil diluted 1:25, given for two months, protected 35 of 39 patients Goldman, *Am. J. Dis. Child.*, 64: 241 (Aug) 1942.

POLYMETHYLENE DIAMINES

Guinea Pigs—

Histamine Antagonism 5, 20, 1, 25, 50, and 0.2 mgm/kg. were minimum protective doses of 2325 RP (N-B-dimethylaminoethyl)-N-ethylbenzylamine), 1571F [B'-(N-ethylanilino)-triethylamine], 2339 RP (N-(B-dimethylaminoethyl)-N-phenyl-benzylamine), atropine, ephedrine and epinephrine respectively against asthma induced by histamine aerosols. Parenterally, the respective LD₅₀'s were—500, 750, 175, 250, 300, and 7 mgm/kg. Previous injection of 5 mgm. 2325 RP, 40 mgm. 2325 RP, and 5 mgm. 2339 RP per kg. completely protected animals against 10, 40-50, and 40 lethal doses of histamine, respectively. Halpern, *Arch. internat. de pharmacodyn. et de therap.*, 68: 339 (Dec) 1942.

POTASSIUM BROMIDE

Man—

Pregnancy Toxemia was treated with 2.5 to 3.0 gm., daily. Thierstein, *J. Kansas M. Soc.*, 43: 49, 1943.

POTASSIUM CHLORATE

Man—

Gingivitis. 0.6 to 0.9 gm. three times daily accelerated beneficial effect of all local treatments Stammers, *Lancet*, 212: 571 (May) 1942.

POTASSIUM CHLORIDE

Mice—

Toxicity: Intraperitoneal median lethal dose to young male albino mice was 6.37 mgm. per 10 gm. mouse administered in 0.2% aqueous solution. Intravenously, 1.0 mgm. per 10 gm. mouse killed 10%, administered as 1% solution. Both intraperitoneal and intravenous toxicities were decreased by simultaneous administration of sodium chloride, but not calcium chloride, glucose or dexamethasone acetate. Emmens and Marks, *J. Physiol.*, 101: 151 (June) 1942.

Man—

Effects of Potassium Salts: Orally, 12.5 to 17.5 gm. potassium chloride or potassium bicarbonate (80 to 100 mgm/kg.) disturbed renal excretion in some normal men. Rapid intravenous injection of 1% potassium chloride led to severe pain in injected vein. When serum potassium concentration reached 30 mgm per 100 ml., after administration of 12.5 gm. potassium chloride, paresthesias in hands and feet resulted, without impairment of heart or kidney function. Keith, Osterberg, and Burchell, *Ann. Int. Med.*, 16: 879 (May) 1942.

Hay Fever in Children: 0.3 gm. three times a day produced notable relief during hay fever season. Stoesser, J. *Lancet*, 62: 174 (May) 1942.

Urticaria: 0.33 gm. three times a day caused improvement in some. Cornbleet, Ingraham, and Schorr, *Arch. Dermat. & Syph.*, 46: 833 (Dec.) 1942.

POTASSIUM FLUORIDE

Rats—

Graded Mottling: Mild mottling resulted with 150 parts per million in diet; mild uniform mottling with concentration of 300 parts per million; and macroscopic hypoplasia with pitting and corrosion at 350 to 550 parts per million. Cheyne, J. *Dent. Research*, 21: 145 (Apr.) 1942.

Man—

Dental Caries in Children: After one year of treatment with topically applied fluoride in 500 parts per million concentration, 3.09 caries were produced and 6.04 caries in controls. Cheyne, J. *Am. Dent. A.*, 29: 804 (May) 1942.

POTASSIUM IODIDE

Mice—

Skeletal Tissues: Injection of 0.1 ml. of 2.5% solution daily for various periods increased proliferation of epiphyseal and articular cartilages, accelerated onset of regression of these cartilages, and stimulated formation and subsequent resorption of bone. Silberberg and Silberberg, *Am. J. Path.*, 20: 329 (Mar.) 1944.

Man—

Toxic Goitre. Adequate preoperative preparation consisted of 0.3 to 1.0 ml. Lugol's solution three times a day, given as soon as a basal metabolic rate had been obtained and for 12 days or longer. Cole, *New Orleans M. & S. J.*, 96: 247 (Dec.) 1943.

Hypersensitivity. 3 ml. Lugol's solution daily for five days, substituted

by 3 ml. potassium iodide daily because of fever and eosinophilia. Two days later, patient had 104.8° F. fever, painful joints, and a generalized papular rash in addition to hemorrhages of buccal and palatal mucosa. Death in three weeks. Typical lesions of periarteritis nodosa were found at autopsy. Rich, Bull. Johns Hopkins Hosp., 77: 43 (July) 1945.

Pulmonary Aspergillosis: Orally, 2.5 ml. of potassium iodide solution three times a day cleared symptoms in nine months. Donaldson, Koerth, and McCorkle, J. Lab. & Clin. Med., 27: 740 (Mar.) 1942.

Syphilis Therapy: 1 gm. in enteric coating containing cetyl alcohol, gum mastic, balsam tolu, gelatin and sugar, was given. Iodine appeared in saliva half an hour after solution or capsule was taken orally, but one and a half hours after enteric coated pill was taken. One pill three times a day to 12 syphilitics was effective in all but one patient (one week to four and a half months treatment). Garfield, New England J. Med., 229: 971 (Dec.) 1943.

POTASSIUM PERMANGANATE

Man—

Fungus Infection: Wet dressing of boric acid or aluminum acetate to hands and arms for 24 hours, soaking of feet and hands in 1:5000 potassium permanganate; calamine lotion 48 hours later, followed by soothing salve. Downing, J. A. M. A., 125: 196, 1944.

Stingarees Wound: Injection of a few minims of 5% solution into puncture and application of cooling lotion or hot fomentations if inflammation occurred. Schultz, U. S. Nav. M. Bull., 42: 750 (Mar.) 1944.

Tropical Dermatoses: Warm compresses of 1:15,000 solution three times a day for 20 minutes were applied to ulcers, and ointment was used at night. Cohen, U. S. Nav. M. Bull., 42: 1119 (May) 1944.

POTASSIUM PHOSPHATE

Man—

Shock Treatment: 1 ml. of potassium phosphate solution (1/6 gram molecule, pH 7.6) into ventricles or cisternal puncture was valuable in laboratory, clinic and war front. Indicated where there was diminution of tone of sympathetic nervous centers, characterized by fall of blood pressure, lowering of cardiac activity and respiration, diminution of excitability and reactivity. Contraindicated in presence of increased excitability of sympathetic nervous system. Stern, Brit. M. J., II: 538 (Nov.) 1912.

POTASSIUM THIOCYANATE

Dogs—

Pathologic Effects: Orally, 0.3 gm. caused prompt fall of blood cholesterol, blood proteins, red cell count, hematocrit value, and hemoglobin. Fatty vacuolization of liver and bone marrow was observed. Blood level was 20 to 60 mgm.%. (In man, 8 to 14 mgm.%). Lindberg, Wald, and Barker, *Am. Heart J.*, 21: 605; 1941.

Man—

Effect on Normals: 0.6 gm. daily caused no fall of blood pressure until seventh day when there was a transient decline of systolic pressure of ten patients. Blood level reached more than 6.0 mgm.% in one week. Lethal dose was 15 gm. as estimated by Nichols (*Am. J. M. Sc.*, 170: 735; 1925), but author's belief is that fatal dose is higher. Quattlebaum, *J. South Carolina M. A.*, 38: 112 (May) 1942.

Fatality: 0.4 gm. daily for a total of 5.6 gm. was taken in 14 days. Highest blood level was 21.6 mgm. Clinical syndrome consisted of profound weakness, mental confusion, toxic psychosis with delirium, hallucinations, and convulsive movements. Russell and Stahl, *J.A.M.A.*, 119: 1177; 1942.

Acute Goutre resulted from taking 1.3 gm. daily for seven months in one patient, and 0.5 gm. daily for four months in another. Subtotal thyroidectomy was performed. Potter, *J.A.M.A.*, 124: 568; 1944.

Hypertension: Optimum therapeutic level was obtained with 0.1 gm. three or four times a day of enteric coated tablets. Blood levels greater than 14 mgm.% were dangerous. Sedlak, *J. Lancet*, 64: 22 (Jan) 1944. Orally, 0.2 gm. once daily, and increased gradually (if toxic reaction was absent) to maintain 12 mgm.% blood cyanate level. Systolic pressure in 70 cases was reduced from 148 to 168 mm. to 118 to 250 mm. Hg and their diastolic pressures from 192 mm. Hg to 156 mm. Hg. Blumenthal and Wetherby, *Minnesota Med.*, 27: 177 (Mar.) 1944. 0.1 to 0.6 gm. daily maintained blood level of 8 to 12 mgm.%, which was effective without toxicity. Tuckwiller, *West Virginia M. J.*, 38: 235 (July) 1942. 0.15 to 1.0 gm. was given daily to maintain 7 to 10 mgm.% in blood. Average blood pressure fall was 46 mm. systolic and 22 mm. diastolic. Ten of 19 patients showed good results. Cannady and Allen, *Illinois M. J.*, 82: 146 (Aug.) 1912. 0.2 gm. was given three times daily for one week, then blood level determined. If it was much above 6 mgm.%, dosage was reduced to 0.4 gm. one day and 0.2 gm. the next, or 0.2 gm. every day. Quattlebaum, *J. South Carolina M. A.*, 38: 112 (May) 1942. 50% effective therapy was

obtained with 0.3 to 0.6 gm. daily in divided doses. Leech, Rhode Island M. J., 25: 84 (Apr.) 1942.

0.3 gm. was given daily in liquid or tablet form. Dosage varied according to patient's symptoms, blood pressure, and blood cyanide determination. Blood level of 8 to 12 mgm/100 ml. gave best relief. Symptoms of toxicity were hemiplegia, delirium, hallucination, depression, word aphasia, unsteady gait and disorientation, fatigue, secondary anemia, and dermatitis. Disappeared on drug withdrawal. Improvement resulted in two to four weeks to three months. Barker, Lindberg, and Wald, J.A.M.A., 117: 1591, 1941 100 cases given 0.1 to 1.2 gm. daily, 51 of 100 showed improvement, 40, marked objective and subjective improvement, and eight improved symptomatically without reduction in blood pressure. Satisfactory response was shown in essential cases, not in chronic nephritis with hypertension. Diabetics showed poor response. Royce, J. Oklahoma M. A., 34 515 (Dec.) 1944.

Migraine Therapy 6 to 12 mgm % blood level gave relief, if maintained. Hines and Eaton, Proc. Staff Meet., Mayo Clin., 17: 254 (Apr.) 1942.

Poisoning 0.6 gm. daily for several weeks resulted in delirium, hallucinations, oliguria, vaginal bleeding, and pulmonary infarction. Blood level was 32.2 mgm.%, and blood pressure, 220/120 on fifth day. Weeks, North Carolina M. J., 5: 234 (June) 1944.

Sensitivity 0.4 gm. daily for eight days in hypertensive old woman produced blood level of 7.5 mgm.% on sixth day, and resulted in acute thyroiditis, dermatitis medicamentosa and acute gastro-enteritis. Fahlund, Proc. Staff Meet., Mayo Clin., 17: 289 (May) 1942.

Severe myxedema with acute thyroid enlargement and total deafness resulted from 0.3 gm. taken twice daily for one week and 0.15 gm. three times daily for four months. Kobacker, Ohio State M. J., 38: 541 (June) 1942.

Thrombophlebitis Developed in 10% of patients, unrelated to blood concentration and to stage of treatment. 10% incidence. Koffler and Freireich, Am. J. M. Sc., 207: 374 (Mar.) 1944.

Toxic Side Reactions. Weakness, bitter taste, anorexia, nausea, itching, purpura, dermatitis, mental confusion, and disorientation occurred with blood concentration greater than 15 mgm/100 ml. Rosenbluth, Bull. New York Acad. Med., 20: 557 (Nov.) 1944.

PREGNANCY

Rats—

Six Hour Test: Subcutaneously, 2 ml. of urine was injected into each of two female animals about four weeks old and weighing 30 gm., and asphyxiated six hours later with illuminating gas. In positive cases, ovarian hyperemia was manifested by a reddening of the ovary, and in negative cases, ovaries were small and white. Kaminester, Am. J. Obst. & Gynec., 47: 265 (Feb.) 1944.

Swine—

Diagnostic Chemical Test: To 10 ml. of filtered urine 1.25 ml. 10% zinc sulfate and 1.25 ml. half normal sodium hydroxide were added and centrifuged. 2 ml. concentrated hydrochloric acid was added to supernatant fluid; hydrolyzed ten minutes; cooled to 15° C., and filtered. 12 ml. of benzene or chloroform was added to filtrate. 5 ml. of solvent extract plus 1 ml. concentrated sulfuric acid, heated to 60 to 70° C. for five minutes; cooled and let stand for 30 minutes. Green fluorescence in acid in mixture was positive test. Roth, Mayer, and Bogart, Am. J. Vet. Research, 2: 436 (Oct.) 1941.

PRIVINE

Guinea Pigs—

Toxicity: 1:25,000 or less with cocaine killed same number of animals as cocaine alone, while higher concentration killed 40% more than cocaine alone. LD₅₀ lies between 1 ml. of 1:250 (4 mgm.) and 1 ml. of 1:100 (10 mgm.) per kg. Not as potent as epinephrine as vasoconstrictor. Craver, Proc. Soc. Exper. Biol. & Med., 58: 128 (Feb.) 1945.

Dogs—

Circulatory Effects: Minimal pressor dose $1-2 \times 10^{-5}$ mm/kg. Maximum response was obtained with 5×10^{-5} to 10^{-4} mm/kg. in dogs narcotized with pentobarbital. Tachyphylaxis at about this dose. Emerson, J. Pharmacol. & Exper. Therap., 82: 42 (Sept.) 1944.

Margin of Safety was high. Effective dose was 5 microgram, and 1 mgm. did not kill. Craver, Chase, and Yonkman, J. Pharmacol. & Exper. Therap., 82: 275 (Nov.) 1944.

Man—

Sedation. Intranasally, five drops of 0.1% prinine hydrochloride three times a day produced several hours of drowsiness after each administration in a girl. Two drops of 0.05% prinine hydrochloride induced eight hours of sleep in a three months' old infant. Orally, 7 to 8 ml. of 0.05%

prinine hydrochloride caused several hours of drowsiness in a three year old. Waring, J.A.M.A., 129: 129, 1915.

PROCAINE

Mice—

Antisulfanilamide Action Subcutaneously, 0.15 gm/kg (maximum non-toxic dose of procaine) in 1:50,000 epinephrine solution was administered at two hour intervals to hemolytic streptococcus infected animals. De Waal, Kanaar, and McNaughtan, Lancet, 2: 724, 1942.

Mice (white)—

Toxicity M.L.D. was 330 mgm/kg intraperitoneally. Co Tui et al., Anesth. & Analg., 22: 301, 1943

Rats—

Toxicity 200 mgm/kg intraperitoneally caused deaths in 20%, 300 mgm/kg. caused deaths in 80%. Repeated intraperitoneal injections at one or two day intervals increased susceptibility rather than tolerance. Schamp, J. Dent. Research, 20: 425 (Oct) 1941.

Rabbits—

Slough Prevention 5 ml of 1% procaine hydrochloride solution in isotonic saline prevented tissue reaction from injection of 5 ml. of 2.5, 5.0, and 10% pentothal sodium solution. Elder and Harrison, J.A.M.A., 125: 116; 1944.

Toxicity Intraspinal minimal lethal concentration was 6% Co Tui et al., J. Pharmacol. & Exper. Therap., 75: 137 (June) 1942.

Laboratory Animals—

Toxicity 100 mgm/kg plus 300 mgm calcium levulinate/kg. prevented convulsions in guinea pigs. 300 mgm calcium levulinate/kg. raised LD₅₀ of procaine from 200 mgm/kg to 450 mgm/kg in rabbits. Similar concentration of sodium bisulfite reduced convulsive dose to one-sixth in rats and one-half in mice. Richards and Kueter, Anesth. & Analg., 22: 283, 1943

Cats—

Toxicity In animals premedicated with pentobarbital sodium, minimal lethal concentration was 35%, and minimal anesthetic concentration was 0.9%. Minimal lethal concentration for the rabbit was defined by Bieter as lowest concentration in per cent, which was fatal in a volume of 0.02 ml. per centimeter spinal length in six out of eight animals (same definition applied to cat here). Minimal anesthetic concentration was defined by Bieter as the lowest percentage solution which caused sensory

anesthesia in six out of eight animals. Co Tui et al., J. Pharmacol. & Exper. Therap., 75: 137 (June) 1942.

Dogs—

Action with Epinephrine: 2 to 4 mgm/kg. injected intravenously had no influence on nasal mucosa or kidney, but dilated blood vessels of hind paw after 20 to 30 seconds lag. When given simultaneously with two gammas of epinephrine, vasoconstrictor effect on kidney and vasodilation effect on hind paw were increased. Administration of mixture into femoral artery caused vasoconstrictor effect of epinephrine to exceed dilator activity of procaine. Cuny and Quivy, Compt. rend. Soc. de biol., 137: 754 (Dec.) 1943.

Toxicity: Mean lethal dose with 2% solution, given intravenously continuously at rate of 5 ml. per minute, was 62.4 ± 14.6 mgm/kg. for unanesthetized animals. Mean lethal dose with 2% solution, using rapid single intravenous injections at 20 minutes' intervals, was 9.7 ± 3.8 mgm. per kg. in animals anesthetized with paraldehyde. Schamp, J. Dent. Research, 20: 425 (Oct.) 1941.

Man—

Analgesic Effect: Maximum rise in cutaneous pain threshold after subcutaneous injection of 100 to 800 mgm. was about ceiling rise observed after aspirin, namely 35% of normal threshold value. Duration of procaine effect was much shorter than aspirin effect. Bigelow and Harris, J. Pharmacol. & Exper. Therap., 81: 368 (Aug.) 1944.

Analgesia for Burns: Intravenous drip of 0.2 to 1.0 gm. as 0.1 to 0.2% solution in saline with 0 to 10% glucose provided excellent selective anesthesia for dressing severe burns in ten patients. Gordon, Canad. M. A. J., 49: 478 (Dec.) 1943.

Antisulfanilamide Action: 30 to 50 ml. of 3% solution had no anti-sulfanilamide action in two patients, nor 60 ml. of 1% solution in third case. De Waal, Kanaar, and McNaughtan, Lancet, 243: 724; 1942.

Bursitis (without calcification): Injection of 20 ml. of 2% hydrochloride solution into bursa and shoulder joint. Guido, California & West. Med., 60: 69 (Feb.) 1944.

Subacromial Bursitis (with calcification): Infiltration with 1% solution under fluoroscopic guidance was treatment of choice. Kaplan and Hawkins, New Orleans M. & S. J., 98: 123 (Sept.) 1945.

Caudal Anesthesia: Injection of 30 ml., 1.0 or 1.5% procaine or metycaine. Volpitto et al., J. M. A. Georgia, 33: 35 (Feb.) 1944.

In proctologic operations more than 15 to 20 ml. of 2% solution in

normal saline at body temperature was given to 3500 patients. There were no deaths, rare failures, no nerve damage or infection. Moon and Christensen, Nebraska M. J., 28: 376 (Dec.) 1943.

Dentistry: 4% procaine hydrochloride with 1:60,000 epinephrine hydrochloride have been used on 500 consecutive patients with success, eliminating insufficient anesthesia occasionally obtained with 2%. Lovestedt, Am. J. Orthodontics (Oral Surg. Sect.), 30: 8 (Jan.) 1944.

Dyspnea Therapy: Intravenously, 5 ml. of 1% solution was given in 75 seconds. Durel, Union méd. du Canada, 74: 1400 (Oct.) 1945.

Gastric Ulcers: Orally, 100 ml. 1% once or twice a day caused immediate subsidence of pain and normalized acidity in patients with gastric and duodenal ulcer. Ulcer niche disappeared in ten to 50 days in most patients. Hamori, Ztschr. f. klin. Med., 142: 406 (Mar.) 1943; through Quart. Rev. Med., 1: 168 (Feb.) 1944.

Herpes Zoster: 10 ml. of 1% solution was slowly infiltrated to block appropriate sympathetic ganglion. Pain disappeared in ten minutes and lesions healed. Findley and Patzer, J. A. M. A., 128: 1217; 1945.

Knee Joint Derangements: One to 3 ml., 1% was injected locally into tender area without a vasoconstrictor in cases where pain persisted for more than a few days. Pickett, Mil. Surgeon, 97: 198 (Sept.) 1945.

Liver Function. Intradural introduction of 150 to 200 mgm. procaine produced least evidence of hepatic dysfunction. Schmidt, Unruh, and Chesky, Am. J. Surg., 57: 43 (July) 1942.

Lobar Pneumonia. 60 to 80 ml. of a 0.5% solution was infiltrated slowly in 20 minutes between third and fourth cervical vertebrae. Speransky and Ginsburg, through Am. Rev. Soviet Med., 2: 22 and 28; 1944.

Local Anesthesia: One and 2% for nerve block and 0.25 and 0.5% for infiltration; total dose should never exceed 1 gm. Anon., Bull. U. S. Army Med. Dept., 4: 271 (Sept.) 1945.

Obstetrical Anesthesia. "Painless labor" of six to ten hours by caudal block anesthesia was obtained with 40 ml. of 2% procaine hydrochloride per injection repeated every two hours. Had greater fetal and maternal safety than any other drug. Hopp, Mil. Surgeon, 89: 675 (Oct.) 1941.

Poliomyelitis: Spinal anesthesia with 100 to 150 mgm. produced significant decrease in muscular spasm in acute and subacute cases. Kabat and Knapp, J. Pediat., 24: 123 (Feb.) 1944.

Posture: Unilateral intensification of spinal anesthesia was secured with posture. In kidney operation, 120 mgm. procaine per 3 ml. cerebrospinal fluid was injected intraspinally with patient lying with diseased

side down. After five minutes position was reversed. Middleton and Middleton, *Rocky Mountain M. J.*, 39: 36 (Jan.) 1942.

Proctologic Work: 30 ml. of 2 or 3% solution was injected into spinal canal. Perkins, *J. Nat. Proct. Assn.*, 17: 118 (June-Aug.) 1945.

Pulmonary Edema Therapy: Spinal anesthesia with procaine hydrochloride, 50 mgm./ml. cerebrospinal fluid brought about marked improvement in three patients. Sarnoff and Farr, *Anesthesiology*, 5: 69 (Jan.) 1944.

Regional Anesthesia: For abdominal and obstetrical and gynecologic operations, level was third space with 100 to 120 mgm. in 3 to 4 ml. spinal fluid; for vaginal work and deliveries 5 mgm., similarly diluted, was injected into fourth space. For sacral block for hypertensive cardiac disease or pre-eclamptic toxemia with respiratory infection, 20 ml. of 2% or 30 ml. of 1% solution was used. For perineal field block, 15 ml. of 1% solution was injected at two points. Waters, *New England J. Med.*, 226: 380; 1942.

Severe Reaction: Immediately after injection into eyelid of 7 ml. of 1% procaine hydrochloride containing one drop of epinephrine per ml. was used in a 73 year old patient, deep cyanosis and stoppage of breathing and heart action occurred. Under artificial respiration, 1 ml. nikethamide intravenously, and 1 ml. 1:1000 epinephrine hydrochloride intracardially; heart started to beat after ten minutes during which time there was no sound of heart action. Lewis, *Am. J. Ophth.*, 27: 293 (Mar.) 1944.

Skeletal Pain: 25% of patients were relieved of muscle and ligament pain by injection at "trigger point" of 1% procaine and 50% of patients by two injections at two to three day intervals. Gorrell, *Am. J. Surg.*, 63: 102 (Jan.) 1944.

Spinal Anesthesia (continuous): 10% procaine was mixed with spinal fluid to give 2.5 or 5% procaine. Initial dose was 50 to 100 mgm., followed by 12.5 to 50 mgm. as needed. Total doses ranged from 50 mgm. to 625 mgm., average was 230.18 mgm. Average dose for hour of anesthesia was 122.46 mgm. Average duration of anesthesia was one hour and 52 minutes, and average systolic blood pressure fall during anesthesia was 22.72 mm Hg. Hale and Shaar, *Anesthesiology*, 5: 53 (Jan.) 1944.

Splanchnic Block: Preoperative sedative was given and epigastric area was anesthetized with a field block of procaine-epinephrine solution which lasted for two hours. After surgical preliminaries, 40 to 60 ml. was injected into peritoneum and upper gastrohepatic ligament. McCorkle, *West J. Surg.*, 53: 51 (Feb.) 1945.

Tolerance: Three patients given 575, 800, and 825 mgm. in 5% solution in subarachnoid space showed no toxicity. Burford, *Anesthesiology*, 3: 159 (Mar.) 1942.

15 gm. (1000 ml. of 1.5%) was tolerated by caudal administration. Minimal effective dose, caudally, was 0.45 gm. (30 ml. of 1.5%). Siever, *J.A.M.A.*, 125: 328; 1944.

PROFLAVINE

Mice (white)—

Experimental Histoplasmosis: Intraperitoneally, 0.05 mgm. daily, starting 24 hours after infection, was of no value. Levy, *Am. J. Trop. Med.*, 25: 211 (May) 1945.

Rabbits—

Tissue Damage was considerable with one part proflavine to 100 sulfathiazole, less with mixture containing 0.5% 0.1% was optimum. Russell and Black, *Brit. M. J.*, 1: 112, 1944.

Man—

Wound Therapy: 1:1000 solution was used and depending on size of wound, 0.2 to 0.5 gm. powder was gently massaged into wound. Raven, *Lancet*, 247: 73; 1944.

PROGESTERONE

Mice (adrenalectomized)—

Protective Action: 500 gammas prolonged life of mice subjected to low temperature. Zarrow, *Proc. Soc. Exper. Biol. & Med.*, 50: 135 (May) 1942.

Rabbits—

Role of Liver: 200 mgm. obtained progestational response comparable to that elicited by 0.25 to 0.5 mgm. subcutaneously, to a normal estrogen-primed animal. Comparable changes were obtained with 25 mgm. in a partially hepatectomized animal. Masson and Hoffman, *Endocrinology*, 37: 111 (Aug.) 1945.

Mammary Glands: 120 international units estrone daily plus 18 doses of 0.25, 1.0, 4.0, 8.0 international units crystalline progesterone were given simultaneously to immature males for four weeks. 1.0 international unit synergized best, though prolactational proliferation was not maximal. 1.0 and 8.0 international units were inhibiting. Lyons and McGinty, *Proc. Soc. Exper. Biol. & Med.*, 48: 83 (Oct.) 1944.

Sublingual Administration: 2 to 8 mgm. progesterone propylene glycol

gave varying response, while 0.5 mgm. progesterone, subcutaneously, produced uniformly positive response. Corner, *Am. J. Obst. & Gynec.*, 47: 670 (May) 1944.

Man—

Abortion (habitual): Prevented by intramuscular injection of 10 mgm. and 10,000 rat units of alpha estradiol benzoate two to three times weekly. Vaux and Rakoff, *Am. J. Obst. & Gynec.*, 50: 353 (Oct.) 1945.

Recurrent and Threatening Abortion: Intramuscularly, daily or on alternate days, 15 to 140 mgm. per week or orally, 20 to 60 mgm. per day of anhydro-hydroxyprogesterone prevented 57% of 16 patients with recurrent abortion and 57% of 30 patients with threatening abortion. Hamblen, *Texas State J. Med.*, 38: 488 (Dec.) 1942.

Functional Uterine Bleeding: Bleeding ceased within ten days of last dose with intramuscular injection of 2 to 10 mgm. of progesterone or 180 to 600 mgm. anhydro-hydroxyprogesterone orally. Ceased in four to eight days in adolescent girls and young women. Allen and Heckel, *Am. J. Obst. & Gynec.*, 44: 984 (Dec.) 1944.

10 mgm. daily for ten days starting on 26th day following onset of withdrawal flow was effective. Smith and Smith, *J. Clin. Endocrinol.*, 5: 319 (Sept.) 1945.

Hemostasis: Initially, 50 mgm. followed by four doses of 10 to 20 mgm. each was for rapid hemostasis. *Ibid.*

Metropathia Hemorrhagia: Injection of 20 mgm. on alternate days for four doses at intervals approximating regular cycle induced normal bleeding and maintained cycle for up to seven years. Dosage was gradually reduced to 5 to 10 mgm. per month. Scowen, *Proc. Roy. Soc. Med.*, 37: 677 (Oct.) 1944.

PROLACTIN

Mice—

Mammary Glands: Subcutaneously, 2 mgm. daily for four to ten days subsequent to parturition showed that a parturitional level of secretory activity continued in mammary tissue for at least five days longer than controls. Williams, *Anat. Rec.*, 93: 171 (Oct.) 1945.

Pigeons—

Bioassay: A method for assay by a comparison of the two crop-sacs of the same pigeon after local, subcutaneous, or intradermal injection. 20% change in dosage detected. Hall, *Endocrinology*, 34: 14 (Jan.) 1944.

Man—

Functional Menorrhagia-Metrorrhagia: Controlled by subcutaneous injection of 100 to 200 international units during each day of bleeding. Hall, J. Clin. Endocrinology, 2: 296 (May) 1942.

PROMIN

(Sodium p,p'-diaminodiphenyl-sulfone-N,N' didextrose sulfonate)

Rats—

Toxicity: Growth was inhibited more by 50 mgm. daily for 21 days on high protein diet than on high carbohydrate diet. Both groups showed alopecia, hyperirritability and anemia 10 gm whole hog liver per day reduced toxicity. Higgins, Am. J. Clin. Path., 14: 278 (May) 1944.

Guinea Pigs—

Experimental Tuberculosis deterred with 400 to 450 mgm. Feldman et al., Am. Rev. Tuberc., 50: 418 (Nov.) 1944.

350 to 450 mgm. daily with feed, starting 42nd day after injection of *M. tuberculosis* gave good results Feldman, Mann, and Hinshaw, Am. Rev. Tuberc., 46: 187 (Aug.) 1942.

400 mgm. orally, and 400 mgm promin nebulized (by inhalation) lengthened survival time Barach, Molomut, and Soroka, Am. Rev. Tuberc., 46: 268 (Sept.) 1942.

Orally, 75 mgm. twice daily (average blood level 4 to 6 mgm/100 ml.) inhibited disease Vaccination increased inhibition. Am. Rev. Tuberc., 48: 453 (Dec.) 1943.

300 mgm. in food (daily) for nine to ten months was effective; but not effective in 21 or 40 day treatment. Armstrong et al., Am. Rev. Tuberc., 50: 160 (Aug.) 1944

Experimental Tuberculosis Therapy. Orally, 30 to 40 gm. of feed containing 30 mgm/30 gm. caused 60% of animals to be without lesions. Feldman, Hinshaw, and Moses, Proc. Staff Meet., Mayo Clin., 16: 187 (Mar.) 1941.

140 mgm. in 40% aqueous solution was given by subcutaneous injection three times a day. One-third on controls died. Steinbach and Duca, Proc. Soc. Exper. Biol. & Med., 49: 460 (Mar.) 1942.

Monkeys (M. Malatta)—

Urinary Concretions Six times human dose, intravenously, did not produce urinary concretions Toomey and Takacs, J. Pediat., 18: 10; 1911.

Man—

Blood Levels: 5 gm. (standard dose) was injected intravenously, three

times daily for three days. Blood levels were: 4 mgm.% or more in 72% of patients. 4 to 10 mgm.% was therapeutically satisfactory. Toomey and Dice, *J. Pediat.*, 18: 6; 1911.

Intravenous Drip Method: 15 to 25 mgm. daily for four weeks did not have beneficial effect on 12 patients with pulmonary tuberculosis. Zucker, Pinner, and Hyman, *Am. Rev. Tuberc.*, 46: 277 (Sept.) 1912.

Leprosy: Intravenously, 0.4 to 4.6 gm. daily benefited nearly all of 137 lepers. Schedule consisted of 1 gm. per day starting dose, gradually increased to maximum amount tolerated (optimum dose was 5 gm.). Six daily injections per week were given for two weeks, then a rest period of one week. Faget and Pogge, *Pub. Health Rep.*, 60: 1165 (Oct.) 1945.

Intravenously, 1.0 to 5 gm. daily, six days per week with rest periods of one to two weeks three times a year was given to 22 unselected patients for 12 months or more. Five showed bacterial reversion to negative, 15 improved, six were stationary, and one became worse. Faget et al., *Pub. Health Rep.*, 58: 1729; 1943.

Tuberculous Meningitis: Total doses ranging from 10 gm. to 225 gm. were given to 11 patients. All died. Morrow, Epstein, and Toomey, *Pediat.*, 24: 623 (June) 1944.

Pneumonia and Tuberculosis: Orally, 1.2 to 3.2 gm. was given daily. Hemoglobin reduced in eight to ten days. Reactions were: cyanosis, headache, and restlessness. Hinshaw and Feldman, *J.A.M.A.*, 117: 1066; 1941.

Pulmonary Tuberculosis: Orally, 0.4 gm. daily increased by 0.4 gm. every ten days until maintenance dose of 1.2 gm. was reached. Intravenous dose was 5 gm. in a 40% aqueous solution. Intramuscularly, 5 ml. of 40% solution caused pain but maintained blood concentration. Did not replace other forms of therapy. Dancey, Schmidt, and Wilkie, *Am. Rev. Tuberc.*, 49: 510 (June) 1944.

Renal Tuberculosis. Orally, 0.2 gm. per day was gradually increased to 0.6 gm. per day. No toxic symptoms observed at this level. 0.8 gm. per day increased urinary frequency and nocturia. No improvement. Wang and Gonzalez-Iman, *J. Urol.*, 53: 769 (June) 1945.

Streptococcus Infection: Intravenously, 5 gm. three times daily for three days was beneficial. No synergistic action when used with sulfanilamide. Toomey and Roach, *J. Pediat.*, 18: 1; 1941.

Tuberculosis Therapy: 1.6 to 3.2 gm. daily oral dose was tolerated for eight days. Blood destruction observed. Hall et al., *Proc. Staff Meet., Mayo Clin*, 17: 24 (Jan.) 1942.

PROMIZOLE

(4,2,diaminophenyl-5,thiazolyl-sulfone)

(p-aminophenyl 2 amino-5-thiazyl sulfone)

Rats—

Goutrogenic Action. Orally or intraperitoneally, 5 to 25 mgm. doses daily caused histologic and weight changes in thyroids. Co-administration of 50 mgm thyroxin or desiccated thyroid of 0.025% of diet inhibited this action. Erythrocyte counts and hemoglobin levels were lowered by daily doses of 10 or 15 mgm., 5 mgm. had no effect. Higgins, Am. J. M. Sc., 210 347 (Sept.) 1945.

Basal Metabolic Rate 5, 10, or 15 mgm. daily for one week caused drop of metabolic rate to -6.8%, -7.2%, and -14.5%, respectively, and after six weeks to -10.8%, -23.5%, and -25.4%, respectively. Ibid.

Guinea Pigs—

Experimental Tuberculosis deterred with 200 to 225 mgm. in feed six, ten to 14 weeks after infection, continued to 226th day after inoculation. 19% died as against 80% of controls. 86% of 64 receiving 30 day treatment survived. Tolerance was good, reticulocytes increased; hemopoietic regeneration undiminished. Feldman et al, Am. Rev. Tuberc., 50: 418 (Nov.) 1944.

Man—

Effect. Large doses were given in renal tuberculosis for ten months without bacterial clearance. No benefit was obtained in tuberculosis meningitis. Toxicity consisted of severe anorexia and upper abdominal distress with oral 12 to 16 gm per day, especially when treatment was continued for three to four weeks, but subsided with 8 to 10 gm. per day. No renal damage or detrimental blood effects were observed up to 24 gm per day. Blood concentration of 3 mgm. per 100 ml was typical; 5 to 12 mgm/ml. caused general malaise. Hinshaw, Feldman, and Pfuetze, Ann. Int. Med., 22: 696 (May) 1915.

PROPADRINE HYDROCHLORIDE**Man—**

Action. 50 mgm subcutaneously with 2 ml. of 1% procaine prior to operation had favorable blood pressure and pulse effect without side effects. It was more active and less toxic than ephedrine and did not cause cardiac irregularities. Marvin, Anesth. & Analg., 23: 45, 1915.

PROPAMIDINE

(p,p'-(trimethylenedioxy) bisbenzamidine)

Man—

Clinical Uses. Intravenously, 0.2 gm. for three to five days brought

reduction of tumor mass and disappearance of redness of skin in lymphogranuloma inguinale. Insufflation of powder for three days was effective in trichomonas vaginalis without recurrence in four weeks Hanschell, Tr. Roy. Soc. Trop. Med. Hyg., 37: 82 (Sept.) 1943.

Vincent's Ulceration: 0.1% in methyl cellulose mucilage was ineffective, but propamidine jelly on cotton-wool produced rapid healing. Stammers, Proc. Roy. Soc. Med., 37: 567 (Aug.) 1944.

PROPYLENE GLYCOL

Air—

Concentration Determination: Two liters of air bubbled through 10 ml. of water with aid of sintered glass filter, and analyzed by Lehman and Newman method, which was accurate to within 0.05 mgm. in sample. With very dilute mixture, four to six liters of air were used for each sample. Puck, Science, 95: 178; 1942.

Bacteria Control. 0.2 mgm. per liter air immediately killed air-borne microorganisms at approximately 40% humidity. Air agitation was desirable. Fog formation when concentration exceeded 0.5 mgm. per liter (which was objectionable to room occupants and dangerous because of fire hazard). Bigg, Jennings, and Fried, Am. J. M. Sc., 207: 361 (Mar.) 1944.

Disinfection: 1 gm. vapor in two to four million ml. air produced immediate and complete sterilization of air into which pneumococci, streptococci, staphylococci, and *H influenzae* and influenza virus had been sprayed. Atmosphere containing vapor up to saturation point (0.7 mgm. per liter air or 1:400,000) were invisible, odorless and non-irritating. Robertson et al., J. Exper. Med., 75: 593 (June) 1942.

Vaporization at rate of 0.5 ml/million ml. of air per hour produced and maintained a 90% reduction in mouth-spray air infection in crowded room and in room with one occupant. Diguid and Challinor, Edinburgh M. J., 51: 388 (Sept.) 1944.

Mice—

Influenza Protection. 1:2,000,000 vapor in chamber with 32 mice protected against mouse-adapted influenza virus sprayed in air in broth suspension. Lungs were normal eight days later. 35 control mice died in six to ten days without propylene glycol vapor. Robertson et al., Science, 94: 612 (Dec. 26) 1941.

Rats—

Oxygen Consumption: Five to ten ml. per kg. given gastrically, de-

pressed oxygen consumption from 1.363 ml. to 1.142 ml. per 100 square centimeters per minute at 22° C. Van Winkle, J. Lab. & Clin. Med., 27: 770 (Mar.) 1942.

PROTAMINE

Hens—

Egg Production: 10 gm/45 kg. feed for one year, given to 24 hens, decreased egg production 6.4% in low-production half of year and produced 102.3% of their previous year's record; values for controls were 43.8% and 89.5%, respectively Turner et al., Poultry Sci., 24: 522 (Nov.) 1945.

PROTEIN

Mice—

Toxicity. LD₅₀ of protamine was 91 mgm. as sulfate, given intraperitoneally; LD₅₀ of histone was 255 mgm. as sulfate, intraperitoneally; 1 ml. (30 mgm.) of globin as sulfate per mouse was well tolerated. Reiner, De Beer, and Green, Proc. Soc. Exper. Biol. & Med., 50: 70 (May) 1942.

Man—

Requirement. Daily protein requirement per kilo was: sedentary or active men or women, 1.0 gm., pregnant women, 1.25 to 1.5 gm.; lactating women, 1.5 to 2.0 gm.; infants under one year, 3 to 4 gm.; and older children smaller amounts decreasing with age. Koehne, Ohio State M. J., 40: 213 (Mar.) 1944.

Requirement in Seriously Ill. 250 severely burned patients had high total urinary nitrogen. Equilibrium existed when urinary output per 24 hours was equal to 90% of nitrogen ingested in that interval. 80 to 125 gm. protein and 2,500 to 3,000 calories per day caused progressive proteinemia. 200 to 300 gm. protein per day required Taylor, Davidson, and Levenson, Connecticut M. J., 8: 141 (Mar.) 1944.

Starvation. 300 gm. protein (not hydrolyzed) and 3,200 calories daily gave best results. Burger, Sandstead, and Drummond, Lancet, 219: 282; 1945.

PROTEIN HYDROLYSATE

Dogs—

Regeneration of Serum Albumin. Intravenously, purified casein hydrolysate increased serum albumin level 18.7% over depletion level caused by diet without nitrogen. Orally, increase was 14.1% given 4 gm/kg. daily for one week. Elman et al., Arch. Surg., 44: 1064 (June) 1942.

Man—

Burn Therapy: Fluid therapy used in patients with burns involved more than 10% of body surface. Intravenously, 10% solution of amino acids or orally in amounts up to 100 to 150 gm. sustained and restored nutrition. Harkins et al., J.A.M.A., 128: 475; 1915.

Enterectomy: Intravenously administered 1.5 liter of 10% dextrose in saline plus one liter Amigen in 5% dextrose daily for 46 days preoperatively and 9 days postoperatively. Recovery. Brunswick, Bigelow, and Nichols, J.A.M.A., 129: 441; 1945.

Gastric Cancer: 2.18 to 2.68 gm. protein per kg. per day was given for ten to 21 days prior to operation to prevent hypoproteinemia. Rasmussen et al., J.A.M.A., 124: 358; 1914.

Nephrotic Toxemia of Pregnancy was treated intravenously with 300 ml. solution containing 45 gm. amino acids. Carr, Wagner, and Hetzer, Am. J. Obst. & Gynec., 47: 70 (Jan.) 1944.

Nitrogen for Burned Patients: Parenterally, casein hydrolysate (15% solution containing 75% amino nitrogen) was given, volume and rate of injection adjusted to comfort of patient. Intrasternally, up to 300 ml. amino acid solution could be administered per hour without discomfort. Taylor, Davidson, and Levenson, Connecticut M. J., 8: 141 (Mar.) 1944.

Nutrition: Intravenously, 50 to 100 gm. hydrolysate maintained positive nitrogen balance. Indicated in starvation states, hepatitis and obstructive jaundice. Lauderman and Weinstein, Surg. Gynec. & Obst., 75: 300 (Sept.) 1942.

Peptic Ulcer Therapy: 300 to 400 gm. daily in eight or nine feedings at two hourly intervals during waking period for two to three weeks and a bland diet thereafter. Co Tui et al., Gastroenterology, 5: 5 (July) 1945.

5 gm. mixed with 5 gm. dextri-maltose suspended in water and given in eight to nine feedings at two hour intervals daily. Co Tui, Bull. New York Acad. Med., 21: 631 (Dec.) 1945.

Postoperative Nourishment. Intravenously, 2.5 to 5% concentration was given in 2.5 to 10% glucose solution. Optimum rate of administration was 8 to 12 gm. of hydrolysate per hour for an average adult. Toxic reactions were urticaria, chills and fever, nausea and vomiting. Elman, Weiner, and Bradley, Ann. Surg., 115: 1160 (June) 1942.

Starvation: Two liters of 7.5 to 10% hydrolysate with equal amounts of glucose daily gave moderate results. Thrombosis followed intravenous injection of 5% acid casein hydrolysate. Burger, Sandstead, and Drummond, Lancet, 249: 282; 1945.

PYRETHRUM

Insects—

Control: 28 gm/500 square feet inside surface was used. Symes, War Med., 2: 340; 1942.

Donkeys—

Tsetse Fly Repellent. Emulsion of 60 ml pyrethrum powder in 300 ml., 2% soft soap solution and water was made to a three liter total. Swabbed or sprayed on, thus protected donkeys from bites of tsetse flies for more than 24 hours. Hornby and French, Tr. Roy. Soc. Trop. Med. & Hyg., 37: 41 (June) 1943.

Man—

Experimental Body Lice Control Powders containing pyrethrins, 2,4-dinitro 6-cyclohexylphenol or 2,4 dinitro-anisole were lethal to lice in clothing of volunteers "MYL" was adopted by Army. Another contained 0.6% 2,4-dinitro-o-cyclohexylphenol, 0.25% pyrethrum concentrate with 20% pyrethrins, and 0.5% N-isobutyl undecylenamide in pyrophyllite dust. Both were effective and safe for skin and clothing for about a week. 30 gm of powder was spread over entire underwear and armpits and crotch of outer clothing. Davis and Wheeler, Am. J. Hyg., 39: 163 (Mar.) 1944

PYRIDOXINE

Colorimetric Determination—

Adsorption on superfiltrol (100 gamma to 0.1 gm. superfiltrol) at pH 3.0. Add butanol solution of 2,6-dichloroquinone chloroimide, adding barbital buffer to pH 7.8 to 8.0 Bird, Vandenbet, and Emmett, J. Biol. Chem., 142: 317, 1942.

Ducks—

Requirement was about 250 micrograms/100 gm. of ration Deficiency caused growth failure and severe microcytic anemia in the young, and paralysis and convulsions in the old Hegsted and Rao, J. Nutrition, 30: 367 (Nov.) 1945.

Rats—

Co-decarboxylase Level 0.1 microgram per mgm dry weight of muscle (pyridoxal units) from animals fed a pyridoxine deficient diet, and 0.1 microgram in those fed 50 micrograms pyridoxine daily. Level was directly proportional to amount of pyridoxine ingested. Umbreit and Gunsalus, J. Bact., 50: 121 (July) 1945.

Deficiency Marked anemia resulted with deficiency. 100 micrograms daily for four days raised low hematocrit levels in two animals. Red blood

cells regenerated slowly. Korenberg, Tabor, and Sebrell, *Am. J. Physiol.*, 143: 434 (Mar.) 1945.

Convulsion (spontaneous) in suckling rats from mothers on pyridoxine deficient diets prevented by 25 to 150 gammas daily to mothers or 10 gammas to young rats. However, no level from 25 to 150 gammas daily prevented sound induced convulsions. Patton, Karn, and Longenecker, *J. Biol. Chem.*, 152: 181 (Jan.) 1944.

Growth: 15 micrograms daily produced maximum growth. Umbreit and Gunsalus, *J. Bact.*, 50: 124 (July) 1945.

Hyperkeratosis and Acanthosis of ears, paws, and snout were treated with single dose of 50 to 100 micrograms, healing in seven to 14 days. Five to ten micrograms daily for two weeks produced permanent healing. Antopol and Unna, *Arch. Path.*, 33: 241 (Feb.) 1942.

Daily Requirement: 10 micrograms. Emerson, *Proc. Soc. Exper. Biol. & Med.*, 47: 445, 1941.

Dogs—

Deficiency: Caused excretion of compound which could be converted to green pigment with ferric ammonium sulfate. Orally, 60 gm. pyridoxine caused disappearance of pigment from urine in 48 hours. Fouts and Lepkovsky, *Proc. Soc. Exper. Biol. & Med.*, 50: 221 (June) 1942.

Man—

Agranulocytic Angina: Intravenous injection of 200 mgm. for several days caused rapid improvement. Cantor and Scott, *Canad. M. A. J.*, 52: 368 (Apr.) 1945.

Cheilosis: Varying doses healed lesions in eight, within three to 14 days. Recurrences successfully treated with subcutaneous dose of 30 mgm. daily. Machella, *Am. J. M. Sc.*, 203: 114; 1942.

Hypocyclosis Therapy: 50 mgm. daily for six days, then every third day for six doses, and finally weekly for six weeks. Clark, *South. M. J.*, 35: 489 (May) 1942.

Muscle Weakness Relief: Intravenously, 50 mgm. of hydrochloride daily. Rosenbaum, Portis, and Soskin, *J. Lab. & Clin. Med.*, 27: 763 (Mar.) 1942.

Muscular Dystrophy: Intramuscular injection of 100 to 300 mgm. of hydrochloride weekly for two to eight months in ten children did not show improvement. Keith, *Am. J. Dis. Child.*, 62: 1327 (Dec.) 1941. Corrected dosage was 100 to 200 mgm. weekly. Keith, *J. Pediat.*, 20: 200 (Feb.) 1942.

Nausea and Vomiting of Pregnancy: One to four injections to maxi-

mum dose of 200 mgm., improved condition. Schwittay, Jackson Clin. Bull., 7: 9 (Jan.) 1945.

Intravenously, 50 mgm. of hydrochloride gave complete relief of nausea with or without vomiting to 38 pregnant women in six to 24 hours. Eight required three to eight injections, 11 required two. Duration of relief was variable. Silbernagel and Burt, Ohio M. J., 39: 1113 (Dec.) 1943.

Intramuscularly, 5 mgm. was injected at two to four day intervals to pregnant women Varas, Bol. Soc. chilena de obst. y ginec., 8: 404; 1943, through Am. J. Obst. & Gynec., 50: 347 (Sept.) 1945.

Radiation Sickness (adjunct to) Intravenously, 25 mgm. of hydrochloride was given immediately after onset to 50 patients. Maxfield, McIlwain, and Robertson, Radiology, 41: 383 (Oct.) 1943; through J.A.M.A., 124: 63; 1944.

Sydenham's Chorea: Dramatic response in three patients administered 180, 425, and 840 mgm. hydrochloride, respectively. Schwartzman, Dragutsky, and Rook, Arch. Neurol. & Psychiat., 48: 141 (July) 1942.

QUINACRINE

Spectrophotometric Determination—

Characteristic sharp absorption peaks at 280 $m\mu$ or 424 $m\mu$ produced by aqueous solution of drug buffered with equivalent volumes of 1.0 N acetic acid and 0.5 N sodium hydroxide. Bissell, Moeller, and Seif, J. Am. Pharm. A (Scient. Ed.), 34: 291 (Nov.) 1945.

In Vitro—

Toxicity: Quinacrine in molar concentration of 1 times 10^{-3} (4 gammas free base per ml) inhibited activity of cholesterase from human serum (1:15), hemolyzed human red blood cells (1:25) and of unhemolyzed human red blood cells (1:25) to the extent of 65, 50, and 50% respectively. Quinacrine was approximately 200 times as effective as quinine or morphine and 1/100 to 1/200 times as effective as eserine. Waelsch and Nachmansohn, Proc. Soc. Exper. Biol. & Med., 54: 336 (Dec.) 1943.

Pigeons—

Assay: Aqueous solution in a constant volume of 0.02 ml/gm. body weight was introduced into crop of male or female animals, starved for 24 hours. Retching movements or emesis was a positive response. ED_{50} for two assays of a sample were 89 and 93 mgm/kg., and in eight assays of another sample values ranged 67 to 100 mgm/kg. (average 83 mgm. per kg.). Thompson and Werner, J. Am. Pharm. A (Scient. Ed.), 34: 231 (Sept.) 1945.

Mice—

Distribution: Intraperitoneally, 2 mgm. as a 2% solution to a total of four to 12 mgm. revealed greatest concentration in liver, spleen, and kidneys. Jailer, Science, 102: 258 (Sept. 7) 1945.

LD₅₀: Subcutaneously, 0.84 to 0.98 gm/kg. atabrine base (disulfate, dilactate, dimethane, dihydrochloride equally toxic); intraperitoneally, 0.19 to 0.25; intravenously, 0.02 to 0.03; orally, 0.83 to 0.75 gm/kg. atabrine in sesame oil, 0.7 atabrine dihydrochloride. Barlow et al., J. Lab. & Clin. Med., 30: 20 (Jan.) 1945.

Rats—

Distribution and Excretion: When 225 mgm/kg. was given as single dose, appreciable amount was found two weeks later; livers contained highest amount. 12 daily doses of 45 or 90 mgm/kg. for one, six, or 13 days showed mottled livers. Intermediate concentration of drug found in spleen, kidney, bone marrow, and walls of small intestines. Urinary excretion with 225 mgm/kg. dose produced 0.25 mgm. quinacrine per rat per day. Amount diminished after eight days but continued for another week. Blood concentration never exceeded 1 mgm.% even after administration of large, multiple doses. Scudi and Hamlin, Proc. Soc. Exper. Biol. & Med., 54: 127 (Oct.) 1943.

Effect: 40 to 65 mgm/kg. per day retarded growth 20 to 35%. 65 mgm. per 100 gm. ration prevented hemorrhagic kidneys in rats on low choline diet. 40 mgm/100 gm. ration prevented death in animals on low choline diet. Hegsted et al., J. Nutrition, 27: 141 (Feb.) 1941.

Excretion: 2% excreted in 48 hours in urine, 90% as unchanged quinacrine, after oral administration of 25 mgm/kg. Scudi and Jelinek, J. Biol. Chem., 152: 27 (Jan.) 1944.

Protein Diet Effect: 45 mgm/kg. caused liver necrosis in 95% of 21 rats on low protein diet and 44% of 18 on high protein diet (30% casein). Loss of weight and myocardial damage was greater in latter group. Thiamine deficiency had no effect. Siegel, Mushett, and Emerson, Proc. Soc. Exper. Biol. & Med., 58: 157 (Feb.) 1945.

Urinary Porphyrin: 45 mgm/kg. per day, given by stomach tube to nine rats did not increase urinary porphyrin, nor in nine animals given 90 mgm/kg., orally. Scudi and Hamlin, Proc. Soc. Exper. Biol. & Med., 54: 127 (Oct.) 1943.

Rabbits—

Picrotoxin: 0.3 mgm picrotoxin per kg. administered simultaneously with 8 mgm. quinacrine per kg. in 90 seconds saved 13 of 18 animals;

without picrotoxin 13 of 15 died. Unna, J. Am. Pharm. A. (Scient. Ed.), 34: 20 (Jan.) 1945.

Cats—

Coccidiosis: 10 cgm/kg. as 1% solution given by esophageal sound for five days gave favorable results. Cats, dogs, rabbits, pigeons, and chickens tolerated 10 cgm/kg. Brumpt, Compt. rend Soc. de biol., 137: 144 (Mar.) 1913.

Infusion Toxicity: Average fatal doses for following rates of infusion were: 53.3 mgm. for 3 mgm/kg per minute, 67.4 mgm. for 2 mgm/kg. per minute, and 116 mgm for 1.0 mgm/kg per minute. Intravenously, 2 mgm. atropine prior to 2 mgm/kg per minute infusion increased tolerated amount to 98.3 mgm Unna, J Am Pharm A. (Scient. Ed.), 31: 20 (Jan.) 1945

Dogs—

Excretion: 5% was excreted in urine, 25% of which was quinacrine, after oral administration of 10 mgm/kg Scudi and Jelinek, J. Biol. Chem., 152: 27 (Jan.) 1944.

Injection Rate. Intravenously, 200 mgm/kg. in one and a half to two minutes caused immediate collapse and death, convulsions, muscular incoordination, stupor and respiratory irregularities. Same dose, given in four minutes, caused staggering and incoordination for 20 minutes. Intravenously, 12 mgm. in two minutes followed two hours later with 12 mgm. was without effect. Infusion at 1 mgm/kg. per minute caused death after 45 minutes from respiratory failure. 50 mgm/kg. was tolerated with infusion at 0.5 mgm/kg per minute, 75 mgm/kg. produced temporary stupor, 100 mgm/kg. was tolerated at 0.4 mgm. per minute. Unna, J. Am. Pharm. A (Scient. Ed.) 31: 20 (Jan.) 1945.

Toxicity: 25 to 50 mgm/kg daily produced manition within three to six weeks. At 5 to 10 mgm/kg this was not evident in three to five months. Plasma fibrinogen levels were more rapidly increased in protein depleted dogs. Scudi and Hamlin J Pharmacol & Exper. Therap., 80: 150 (Feb) 1914.

Man

Excretion: With oral 100 mgm daily with evening meal, daily urinary excretion gradually increased for three to four weeks, but never exceeded 11% of daily dose Kelsey et al. J Pharmacol & Exper Therap., 80: 383 (Apr.) 1914.

Plasma Concentration When fasting blood plasma levels of 45 micrograms per liter were attained in 24 hours and maintained, symptoms were abolished in practically all cases within 72 to 96 hours. Regardless of

plasma level, 90% of blood smears were negative in 32 to 48 hours of initiation of treatment. Ellerbrook et al., Bull. U. S. Army M. Dept., 87: 34 (Apr.) 1945.

Poisoning: Orally, 25 gm. given to a patient who had received quina-crine suppression therapy for 16 months caused severe vomiting in ten minutes followed by diarrhea, drowsiness, and weakness leading to collapse. Markson and Dawson, Ann. Trop. Med., 39: 117 (Oct.) 1945.

Toxicity: Orally, 2.1 gm. caused psychotic symptoms after sixth day of last dose in 35 of 7604 malaria patients. Gaskill and Fitz-Hugh, Bull. U. S. Army M. Dept., 86: 63 (Mar.) 1945.

Prolonged Use: Orally, 0.1 gm. daily for 11 to 12 months caused no liver or kidney impairment in 1000 cases. No significant hemopoietic changes were observed in 95 patients given 0.4 to 0.7 gm. for four to ten months. Plasma levels of 25 micrograms per liter were reached in five to six weeks and maintained. Macgraith and Havard, Lancet, 249: 141; 1945.

0.1 gm. per day for six days a week taken for four to 18 months by 102 soldiers showed no evidence of liver damage or other ill effects. Drew and Reid, Lancet, 249: 107; 1945.

Orally, 0.4 to 0.7 gm. weekly for four to ten months were given to 65 women and 30 men. There was no significant change in red or white cell counts and hematocrit or erythrocyte sedimentation rate. (Great Britain) Army Malaria Research Unit, Ann. Trop. Med., 39: 133 (Oct.) 1945.

Prolonged Administration: Orally, 0.1 gm. daily over a period of nine to 12 months, given to 43 healthy men, showed no impairment of liver or kidney functions. Great Britain Army Malaria Research Unit, Ann. Trop. Med., 39: 128 (Oct.) 1945.

Liver Function: 0.1 gm., six days a week for 18 to 30 months produced no evidence of subclinical liver damage in 125 soldiers. Gottfried and Levine, J. Lab. & Clin. Med., 30: 853 (Oct.) 1945.

Giardia Lambliia intestinalis (children): Divided doses of dihydrochloride totaling 0.1 to 0.3 gm. daily for three successive days, followed 48 hours later with a large dose of magnesium sulfate cleared 66% of giardia; relapse in 13%; and in 21% therapy failed. Maris and Bushong, Pennsylvania M. J., 45: 724 (Apr.) 1942.

Giardia Lambliia enteritis: Adults were given 0.1 gm. three times a day and children one-sixth of 0.1 gm. tablet three times a day for five days. Stools were negative. Ormiston, Taylor, and Wilson, Brit. M. J., II: 151 (Aug.) 1942.

Leishmaniasis (cutaneous): Early papules destroyed by infiltration with 5% solution, and ulcerating sore by infiltration with 10 ml. of 3% solution or application of 10% ointment. Dobrotvorskaya, Problems of Cutaneous Leishmaniasis, Ashkhabad, 207: 1941; through Trop Dis. Bull., 41: 337 (May) 1944.

Weekly infiltration of one to 3 ml. of 10% for two to three weeks had no effect. Berberian, Arch. Dermat. & Syph., 52: 26 (July) 1945.

Tsutsugamushi Disease. 0.1 gm. daily effected recovery in all of 49 patients. Anderson and Wing, War Med., 8: 163 (Sept.) 1945.

Typhus Fever Therapy: 0.18 gm. three times a day plus plasmochin 0.02 gm. once a day brought striking benefit to seven patients. Van Meern-donk, Deutsche mil.-arzt. Zschr., 7: 283 (Apr.) 1942; through Bull. War Med., 3: 217 (Dec.) 1942.

Malaria Therapy in the American Tropics First period. quinacrine in 0.1 gm. doses three times daily during the febrile period and for four days thereafter; second period: 0.32 gm. quinine sulfate four times daily for seven days; third period. 0.1 gm. quinacrine three times daily for five days; fourth period: 0.32 gm. quinine sulfate three times daily for five days; fifth period 0.32 gm. quinine sulfate and 0.01 gm. Plasmochin three times daily for five days. Dove, Am. J. Trop. Med., 22: 227 (May) 1942.

Subtertian Malaria Therapy. Intramuscularly, 0.5 gm. at once in all pernicious attacks in which vomiting was complication, again after six hours, and also if necessary in next 24 hours. Drug was then given orally three times a day for three days. Gerrard, Brit. M. J., I: 196 (Feb.) 1944.

Plasmodium Vivax Malaria 0.1 gm. daily for two months after clinical treatment of each recurrence greatly increased time interval between relapses and decreased number of relapses in 63 men. Lewis and Kibbe, Bull. Johns Hopkins Hosp., 77: 211 (Sept.) 1945.

Malaria. Initial dose of 0.8 gm. was given during first 24 hours of treatment. 0.3 gm. daily were capable of dealing with small numbers of parasites in blood stream. No toxic reaction with 0.6 gm. weekly as suppressive for six months or more. Findlay, Markson, and Holden, Ann. Trop. Med., 38: 139 (Sept.) 1944.

Benign Tertian Malaria 0.3 gm. three times on first day (0.2 gm. in Indian troops), 0.2 gm. three times on second day, and 0.1 gm. three times on third to seventh day, were followed by 0.1 gm. daily for at least six weeks. If there were more than three benign tertian attacks in one year, 0.65 gm. quinine three times a day for ten days together with 0.01

gm. plasmochin three times a day for British troops and twice a day for Indian troops were given. Marriott, *Lancet*, 1: 679; 1945.

0.1 to 0.2 gm. six days a week for five to seven weeks, beginning one to two weeks before multiple exposure to infected mosquitoes protected against *P. falciparum* but not *P. vivax*. 0.1 gm. twice a day on two non-successive days weekly for two to six weeks, starting one day before a single exposure, protected against *P. falciparum*. Boyd and Kitchen, *Am. J. Trop. Med.*, 25: 307 (July) 1945.

Malaria Suppression: 0.1 gm. daily suppressed malignant tertian fever. Fairley, *Tr. Roy. Soc. Trop. Med. & Hyg.*, 38: 311; 1945.

Malaria: 0.1 gm. daily was given as a suppressive dose. 0.3 gm. daily for one week followed by suppressive dose when parasites were found in blood, even though no symptoms were present. Mistachkin, *U. S. Nav. M. Bull.*, 44: 916 (May) 1945.

Relapse Management: Medication should be taken with regularity. Not more than 5% of those taking 0.1 gm. quinacrine daily suffered from relapses. Anon., *Bull. U. S. Army M. Dept.*, 87: 33 (Apr.) 1945.

Concurrent Use of Sulfas: 2 gm. quinine daily for four days, 59.5 gm. sulfadiazine in 12 days, 0.1 gm. quinacrine daily for 22 days, and 200,000 units type VII antipneumococcus rabbit serum intravenously were given for a case of pneumonia without harm. Bercovitz, *Ann. Int. Med.*, 23: 79 (July) 1945.

QUINIDINE

Man—

Auricular Fibrillation: After heart rate was retarded with digitalis, quinidine was given, total daily dose was increased by 0.2 to 0.3 gm. as long as fibrillation persisted. Total daily dose was divided into three to four equal parts and administered hourly during the morning. Berman and Blumenthal, *Minnesota Med.*, 25: 198; 1942.

Therapeutic Dose: Test dose of 0.2 gm. was followed by 0.4 gm. every two hours until regular rhythm was restored, then maintenance dose was given. Administered intramuscularly or orally; intravenous use was dangerous. In 75 to 90% regular rhythm was restored. Indicated in arrhythmia in young with little heart damage, arrhythmia after an acute infection or operation, mitral disease with persistent extra-systoles. Contraindicated in severe cinchonism, acute infection, bacterial endocarditis, extensive myocardial disease, old age, hyperthyroidism prior to thyroidectomy, angina pectoris, and complete heart block. Carter, *M. Clin. North America*, 29: 215 (Jan.) 1945.

Ventricular Tachycardia: 1.5 gm., the minimum amount in 24 hours; and 34 gm., the maximum amount in nine days terminated arrhythmia in seven of eight. Zimmerman, Ann. Int. Med., 23: 634 (Oct.) 1945.

QUINIDINE LACTATE

Man—

Ventricular Tachycardia: Intravenously, 0.325 to 1.3 gm. effectively relieved attacks and orally, 2 gm. quinidine sulfate per day as a maintenance dose prevented recurrences. Chapman, Am. Heart J., 30: 276 (Sept.) 1945.

QUINIDINE SULFATE

Man—

Auricular Fibrillation. 0.4 gm. every two hours for six or more doses or until normal rhythm was restored, and then dose was reduced to 0.8 gm. every 24 hours in doses of 0.2 gm. four times daily. Limbaugh, J. Florida M. A., 28: 273, 1942.

Ventricular Tachycardia converted to normal rhythm by 0.2 gm. for first dose, increased by 0.1 gm. every two to three hours, and dose at which normal rhythm was restored plus 0.1 gm. was maintenance dose, given four times a day, for 18 to 20 days after onset of infarction. Individual could be given 1.5 gm. without harm. Contraindicated in sensitivity to quinine, chronic auricular fibrillation, etc. McMillan, South. M. J., 36: 800 (Dec.) 1943.

DIHYDROQUINIDINE

Cats—

Comparative Pharmacology 1.0 mgm/kg. dihydroquinidine and 3.5 mgm/kg. quinidine were required to raise intensity of electric stimulation needed to produce ventricular fibrillation. Intravenous median lethal dose was 18% more toxic than quinidine. Intravenously, 10 mgm. per kg. caused marked fall of blood pressure. Scott, Anderson, and Chen, J. Pharmacol. & Exper. Therap., 84: 184 (June) 1945.

QUININE

Birds—

Experimental P. gallinaceum Infection: A total of 150 gm. of quinine hydrochloride per kg. given daily caused young gametocytes to form directly from merozoites of extra-erythrocytic origin within 27.5 hours of cessation of drug. Adler and Tchernomoretz, Nature, 153: 83 (Jan.) 1944.

Canaries—

Experimental Avian Malaria: Nine of ten controls did not reach a crisis until fourth day; eight of ten, given 1.0 mgm. bisulfate in 0.1 ml. water three times a day for four days, reached in three or four days; ten of ten, given 0.25 mgm. bisulfate in 0.05 ml. water every two hours for four days, reached it on second or third day. Beckman and Smith, J. Lab. & Clin. Med., 29: 43 (Jan.) 1944.

Chickens—

Metabolism: 216 micrograms was metabolized in two hours by 0.5 gm. liver tissue of ten day old embryo, 26 micrograms by three day old chick, and 730 micrograms by whole chick embryo ten days old. Marshall, Nature, 155: 730 (June) 1945.

Plasmodium gallinaceum: 0.1 to 0.2% in diet immediately suppressed growth and development, and number of parasites dropped below initial count on second day Brackett, Waletzky, and Baker, J. Pharmacol. & Exper. Therap., 84: 254 (July) 1945.

Dogs—

Distribution: Infusions of sulfates of quinine, quinidine, cinchonine and cinchonidine were made for thirty minutes, and body fluids and tissues analyzed for alkaloid content. Ratio of tissue concentration to plasma concentration was low (0.1 to 5.0) for red blood cells, cerebrospinal fluid, skeletal muscle and brain, high (10 to 40) for glandular tissues and lung. Hiatt and Quinn, J. Pharmacol. & Exper. Therap., 84: 101 (Feb.) 1945.

Metabolism: Orally, 0.2 to 0.4 gm., one to six times daily, decreased excretion of total nitrogen, urea nitrogen, phosphorus, inorganic sulfur and chlorides. Creatinine, creatine, vitamin C, ammonia, amino acid nitrogen, and organic sulfur were unaffected. Milhorat, Bartels, and Toscani, Proc. Soc. Exper. Biol. & Med., 48: 540 (Nov.) 1941.

Man—

Bronchomoniliasis: 0.3 gm. twice a day for two and a half weeks gave good results to young Canadian gold miner. Farrell, Canad. M. A. J., 48: 28 (Jan.) 1943.

Gramps (night): 0.02 to 0.32 gm. nightly completely relieved 17 of 24 in seven days. Nicholson and Falk, New England J. Med., 233: 556 (Nov.) 1945.

Hypothrombemia. Caused by 0.33 gm. of sulfate given orally, daily for six to 16 days in five normal individuals. Pirk and Engelberg, J. A.M.A., 128: 1093; 1945.

Idiosyncrasy: Man taking 0.1 gm. quinine and 0.01 gm. pamaquine had severe attacks of rigor, hyperpyrexia, diarrhea, cramp-like abdominal pains, vomiting and headache. Braun, Czertok, and Kornblueth, Tr. Roy. Soc. Trop. Med. & Hyg., 37: 221 (Dec.) 1913.

Intravenous Injury: 20 of 21 patients receiving five intravenous injections of 0.3 to 0.6 gm. of hydrochloride in graded doses to total of 2.6 gm. showed varying degree of myocardial impairment. Heilig, Indian M. Gaz., 79: 514 (Nov.) 1914.

Malaria: For men from malarious areas, salt of quinine was given orally 0.65 gm. three times daily for two days; quinacrine hydrochloride 0.1 gm. orally, three times daily for five days, two days interval, then pamaquin, 0.01 gm. three times daily for five days. Great Britain War Office, Pamphlet, 1911, through Lancet, 211: 567 (Nov.) 1911.

One daily dose of 2.0 gm. about two hours before expected rigor gave best results. Marshall, Brit. M. J., II: 236 (Aug.) 1912.

Intramuscularly, 0.4 gm. daily for 30 to 50 injections saved quinine and shortened course of malarial attack. Hall, Brit. M. J., II: 559 (Nov.) 1912.

Intravenously, 0.65 gm. in 20 ml. given in five minutes produced no untoward reaction in 5000 patients. Taken orally thereafter. Turner, Lancet, 217: 737; 1914.

Intramuscularly, 2 ml. of solution containing quinine dihydrochloride and phenazone, twice a day for four days, followed by 0.1 gm. quinacrine three times a day for seven days and then 0.01 gm. pamaquin three times a day for three days, produced satisfactory results in subtertian malaria. Cooke and Wingfield, Lancet, 216: 801, 1911.

Malignant Malaria Intravenously, 0.65 gm. in 200 ml. normal saline injected in 15 minutes, or quinacrine 0.1 gm. in 10 ml. very slowly. Intramuscularly, 0.65 gm. quinine hydrochloride in 2 ml. water or 1.0 gm. in 3 ml. or 0.2 or 0.4 gm. quinacrine in five or 10 ml. of water. Only first dose should be given intravenously. Average daily dose was 2 gm. quinine (maximum 3 gm.) or 0.3 gm. quinacrine (maximum 0.6 gm. or more). Quinine was given every six to eight hours, quinacrine every 12 to 24 hours. Kneedler, Clinics, 3: 809 (Dec.) 1913.

Malaria Prevention 0.65 gm. daily failed to prevent overt attacks of malignant tertian malaria. 0.3 gm. daily was incapable of preventing benign tertian malaria attacks but 0.65 gm. daily caused complete suppression in some. Fairley, Tr. Roy. Soc. Trop. Med. & Hyg., 38: 311; 1915.

Primary Atypical Pneumonia 0.1 to 0.65 gm. daily gave better im-

provement and quicker results than those denied drug. *Feinblatt, Indust. Med.*, 14: 517 (June) 1915.

Poisoning (in child four years): 1.04 gm. was given in malaria treatment. Signs and symptoms of hemorrhagic purpura. Controlled within a month with liver extract, vitamin K and diet abundant in milk and fruit juices. *Pinos, Bol. Soc. cubana de pediat.*, 14: 49 (Feb.) 1912; through *J.A.M.A.*, 119: 846; 1942.

Atypical Reaction: 0.65 gm. three times a day (8 gm. in four days) caused rash, edema, and urticaria. *Greene, Mil. Surgeon*, 97: 61 (July) 1945.

Respiratory Infection: 0.3 gm. four times a day gave symptomatic relief with marked antipyretic and analgesic effect in upper respiratory infection and measles. *Cowan, South. M. J.*, 36: 798 (Dec.) 1913.

Sodium Bicarbonate: Maintenance of alkaline urine with sodium bicarbonate, by halving quinine excretion, reduced quinine dosage by one-half. *Hoag and Schwartz, South. Hosp.*, 12: 49 (Feb.) 1914.

QUINOLINE DERIVATIVES

Pigeons—

Haemoproteus columbae Infection: Orally, 0.5 to 25 mgm. of 6-methoxy-8 (γ -diethyl-aminopropylamine) quinoline methylene-bis-salicylate in glucose solution, given in single daily doses, was the most effective of quinoline and acridine derivatives against gametocytes. *Bos and Rakshit, Quart. J. Pharm. & Pharmacol.*, 17: 319 (Oct.-Dec.) 1944.

RELAXIN

Guinea Pigs—

Assay: One unit was the amount producing definite relaxation of symphysis pubis, six hours after injection in 60% of animals weighing 250 to 350 gm and pre-treated by ovariectomy and injected with 0.83 mgm. estradiol daily for four days. *Abramivitz et al., Anat. Rec.*, 84: 456 (Dec.) 1942.

RENIN

Dogs—

Blood Pressure Restoration: 10 to 25 ml. renin activator of ox plasma injected after experimental hemorrhage produced 15 to 80 mm. Hg rise and lasted 20 to 120 minutes. *Sapirstein, Southard, and Ogden, Proc. Soc. Exper Biol & Med*, 50 320 (June) 1942.

Hypertension: Intramuscularly, purified renin daily an equivalent of 1.0 gm. of fresh kidney cortex per kilo body weight, given for four months

or until animal died, did not affect blood pressure. Friedman, Kruger, and Kaplan, *Proc. Soc. Exper. Biol. & Med.*, 50: 56 (May) 1942.

Renal Ischemia Intramuscularly, hog renin in doses representing one gram of kidney equivalent per kilo body weight for four months reduced blood pressure. Wakerlin et al., *Science*, 93: 332, 1941.

RIBOFLAVIN

Chicks—

Requirement. 250 micrograms for maximum growth to eight weeks, and more than 300 micrograms per 100 gm ration was required for curled toe paralysis prevention. Bethke and Record, *Poultry Sci.*, 21: 147; 1942.

Turkey Poults—

Requirement: 270 micrograms per 100 gm ration was required for normal development during first six weeks of life. Patrick, Darrow, and Morgan, *Poultry Sci.*, 23: 146 (Mar.) 1944.

Rats—

Excretion: By stomach tube, 10 or 40 micrograms was given to male rats fed riboflavin deficient diet. Total output was proportional to amount of fecal excretion. Content in stools did not decrease as avitaminosis progressed. Obermeyer, Wurtz, and Emerson, *Proc. Soc. Exper. Biol. & Med.*, 59: 300 (June) 1945.

Dogs and Rats—

Urinary Excretion: Subcutaneously injected doses excreted in urine averaged 74, 28, and 12% respectively, on low, medium, and high protein intake. Casein content was 2.6, 17.6, and 4.1% of total calories. Sarett, Klein, and Perlzweig, *J. Nutrition*, 24: 295 (Sept.) 1942.

Dogs—

Requirement: Minimum requirement was 200 micrograms per 100 gm. of ration, and 400 micrograms per 100 gm of ration for growing dogs. Axelrod et al., *Am. J. Physiol.*, 133: 555; 1941.

Horses—

Iridocyclitis. 40 mgm. per horse per day added to diet of 130 horses with annual rate per 1000 of new cases of iridocyclitis of 109.56 resulted in no new cases of disease for that year. Jones, *Mil. Surgeon*, 96: 310 (Apr.) 1945.

Monkeys—

Deficiency. Treatment with 50 gammas per day caused remission of symptoms in mild cases within two to three weeks, 100 to 500 gammas per day for ten to 14 days for severe cases. Waisman, *Proc. Soc. Exper. Biol. & Med.*, 55: 69 (Jan.) 1944.

Monkeys (rhesus)—

Requirement was 25 to 30 micrograms/kg. for young monkeys. Deficiency caused loss of weight in six to eight weeks, extensive freckled type of dermatitis, decrease in hemoglobin, red blood cells and white cells, a hypochromic normocytic type of anemia. Urinary excretion dropped ten to 15% of daily intake. Fatty livers. Cooperman et al., J. Nutrition, 30: 45 (July) 1915.

Man—

Dermatology: Five to 15 mgm. daily had special value in cheilosis and was probably specific in rosacea keratitis. Novy, California & West. Med., 56: 144 (Mar.) 1942.

Ophthalmology: Orally, 15 mgm. was given. In severe cases 5 mgm. was also given intravenously. For marginal keratitis, marginal catarrhal ulcers of the cornea, and corneal erosions. Clark, South. M. J., 35: 489 (May) 1942.

Restricted Riboflavin Diet: No physiologic handicap was observed from subsistence for five months on diet providing 0.31 mgm/1000 calories in young, normal men. Keys et al., J. Nutrition, 27: 165 (Feb.) 1944.

Parenteral Use: Three to 4 mgm. daily for the ill. If patient had been subjected to deprivation, then 10 mgm. for five days would compensate for depleted stores. Ingelfinger, New England J. Med., 233: 379 (Sept.) 1945.

RICINOLLATE, SODIUM**Monkeys—**

Peritoneal Adhesion Prevention: 3 ml/kg. of 0.25 to 4.0% solution was given intraperitoneally. Animals sacrificed at intervals of 24 hours to 21 days. Degree of inflammation and length of time it persisted was proportional to concentration of drug in distilled water. Seeley, Am. J. Surg., 56: 579 (June) 1942.

ROTENONE**Rats—**

Large Doses: 125 to 500 mgm/kg. as 2.5% solution in saline, injected intraperitoneally, precipitated vitamins in kidneys and urinary tract, sometimes followed by urinary obstruction, uremia, and a calcifying nephrosis. Antopol, J. M. Soc. New Jersey, 39: 285 (May) 1942.

Cattle—

Hornfly Control: Orally, minimum dose that killed all hornfly larvae was 0.4 gm/cwt. Minimum effective dose was 0.3 gm/cwt. administered

daily. Bruce, J. Kansas Entomol. Soc., 13: 41; 1941; through Exper. Sta. Rec., 84: 222; 1941.

Man—

Scabies: 85% responded in 50 patients treated with local application of preparation containing 2% rotenone in mucilage of quince seeds, Irish moss and chloroform Epstein, Arch. Dermat. & Syph., 45: 950 (May) 1942.

SACCHARIN

Man—

Circulation Time (arm to tongue): Anticubital vein was punctured, tourniquet released, needle left in place one minute for circulation readjustment. 2.5 gm saccharin in 2 ml water was quickly injected. Time between injection and patient's announcement of sweet taste was measured. Duras, Lancet, 246: 303, 1944.

SALICYLANILID

Man—

Five per cent concentration in carbowax 1500 cleared 57% of children infected with *Tinea capitis* who received 38 to 40 treatments. Continued treatment raised the percentage cleared to 98 Schwarz et al, Pub. Health Bull., # 294; 1946.

SALICYLATES

Man—

Optimum Dosage. In rheumatic fever and atrophic arthritis orally, 195 to 220 mgm. of sodium salt per kg. was given with one-third that amount of sodium bicarbonate. Plasma salicylate level should be 350 micrograms per ml. Side effects easily controlled. Lawson, North Carolina M. J., 5: 477 (Oct.) 1941.

Rheumatic Fever Therapy. Orally, 10 to 12 gm. per day, but up to 20 gm. daily was tolerated. Sedimentation rate did not return to normal for three to six weeks with blood levels of 35 mgm/100 ml. Wright, Bull. New York Acad. Med., 21: 119 (Aug) 1945.

Large doses of salicylates were given to raise plasma level to 350 to 450 gammas per ml. for children with rheumatic polyarthritis. Taran and Jacobs, J. Pediat., 27: 59 (July) 1945.

Toxic Reactions. 300 gammas and 450 gammas per ml., respectively, of serum salicyl levels in two cases, developed tendon sheath nodules; another with a level between 350 and 265 gammas per ml. developed tenosynovitis; a florid rheumatic pneumonitis developed in a fatal case

with a level above 300 gammas per ml.; and an episcleral nodule developed in the fifth case with a level between 450 and 60 gammas per ml. Murphy, Bull. Johns Hopkins Hosp., 77: 1 (July) 1945. Respiratory alkalosis, pustular acne, and maniacal delirium resulted in patients with plasma salicylate level maintained above 30 mgm.% by giving 10 to 16 gm. sodium salicylate orally or intravenously. Coombs et al., Proc. Central Soc. Clin. Research, 17: 24; 1944. In nine year old negro: Hyperpnea resulted after 40 gm. were given in 6 gm. doses per day for four days, then 8 gm. per day. Nausea and vomiting resulted after 48 gm. were given and disorientation and hallucination after 72 gm. Fashena and Walker, Am. J. Dis. Child., 68: 369; 1944.

SALICYLIC ACID

In Vitro—

Determination in Plasma: Salicylate was extracted with ethylene dichloride and the ethylene dichloride solution treated with 1% ferric nitrate in 0.07 N nitric acid. Color formed was read in colorimeter using a filter with a maximal transmission at 540 millimicron. Brodie, Udenfriend, and Coburn, J. Pharmacol. & Exper. Therap., 80: 114 (Jan.) 1944.

SCOPOLAMINE

Man—

Airsickness: Given one-half to one hour pre-flight had preventive effect of at least four hours duration. Lilienthal, Science News Letter, 46: 179; 1944.

Labor: 0.4 gm. had no effect on amplitude, slightly prolonged interval, and diminished tonus of uterine contractions. 1.2 mgm. abolished uterine motility. Bickers, Virginia M. Monthly, 69: 15 (Jan.) 1942.

Seasickness: 0.6 mgm. one hour before embarking caused sickness in 20% of 218 and 47% of 212 untreated; and with 1.2 mgm., 14% of 84 men and 51% of untreated. Scopolamine was most effective of a number of drugs. Dryness of mouth was only side effect. 0.6 mgm. as initial dose, followed by 0.3 mgm. every six hours for 48 hours produced no ill effects. Holling, McArdle, and Trotter, Lancet, 246: 127; 1944. Prophylactic: 0.6 mgm., one-half hour before sailing, repeated in four hours, then every six hours thereafter. Dose decreased gradually after third day. Curative: Subcutaneously, 0.8 mgm. with 8 mgm. morphine, then continued orally as above. Gilbert, Brit. M. J., I: 70 (Jan) 1945.

Toxicity. Intramuscularly, 0.6 mgm. with 100 mgm. Demerol followed by 100 mgm. Demerol every hour and 0.4 mgm. or 0.3 mgm. scopolamine

three-quarters to two hours, respectively after initial dose had been discontinued resulted in three instances of massive edema of uvula and glottis. Steinberg, Am. J. Obst. & Gynec, 50: 542 (Nov.) 1945.

SECONAL SODIUM

Man—

Fatality: 0.9 gm. found in stomach content, 24 mgm/800 ml. of urine, and none in blood. Wheelock and Freedman, J.A.M.A., 129: 130; 1945.

Rectal Administration (in children): 0.006 gm/kg., for examination of unruly child; 0.012 gm/kg. for painful procedures such as spinal punctures and paracentesis. Breslow and Poncher, Illinois M. J., 80: 210 (Sept.) 1941.

SELENIUM

Rats—

Toxicity: Three to 40 parts per million in grain diet showed toxic effects at all levels. Ten parts per million and more than ten parts per million killed most of animals in eight weeks. Chronic symptoms were decreased growth rate, restriction of food consumption, and pathologic lesions (cirrhosis of liver). Fitzhugh, Nelson, and Bliss, J. Pharmacol. & Exper. Therap., 80: 289 (Mar.) 1944.

SERUM ALBUMIN

In Vitro—

Effect of Stabilizers. Addition of 0.05 M to 0.3 M sodium phenyl acetate caused varying degree of distortion in shape of human red blood cells, but no hemolysis occurred within 24 hours at room temperature. 0.04 M to 0.08 M sodium mandelate caused no hemolysis, and at latter concentration, no red blood cell distortion. Bassett, Am. J. Physiol., 143: 272 (Feb.) 1945.

Stabilizing Agent in Schick Toxin: 0.2% human serum albumin content gave best protection to diphtheria toxin, 0.1% was adequate, and 0.05% insufficient. Edsall and Wyman, Am. J. Pub. Health, 34: 365 (Apr.) 1944.

Mice—

Stabilized Albumin. Intravenously, 3 ml/kg. of phenylacetate or mandelate stabilized preparations caused no deleterious effect. Bassett, Am. J. Physiol., 143: 272 (Feb.) 1945.

Rabbits—

Stabilized Albumin: Intravenously, 3 ml/kg. of 0.05 M phenyl acetate or 0.08 M mandelate stabilized albumin given to two anesthetized rab-

bits caused no change in pulse rate, blood pressure and rate and depth of respiration. Ibid.

Man—

Shock: 20 to 95 gm. in saline or 0.3 M solution of sodium chloride and sodium acetate was given. Amount retained after one to six hours was 8 to 73 gm., and average blood volume increase per gm. of albumin retained was 23 ml. Cournand et al., J. Clin. Investigation, 23: 491 (July) 1944.

25 gm. concentrated normal serum albumin from man in 100 ml. diluent was equivalent in osmotic effect to 500 ml. citrated plasma and was used to restore blood volume. Repeated injection to 600 patients caused no evidence of sensitization. A hypoproteinemia patient assimilated 25 gm. per day. Janeway et al., J. Clin. Investigation, 23: 465 (July) 1944.

SERUM, ANTI-RETICULAR CYTOTOXIC

Man—

Adjunct of Routine Therapy: 0.5 to 0.75 ml. serum, diluted ten times, was given subcutaneously at three to four day intervals. Linberg, through Am. Rev. Soviet Med., 1: 124 (Dec.) 1943.

Use: Powerful specific factor influencing physiologic system of connective tissue. Indicated for use in frostbites and wounds; infectious diseases including spotted fever, puerperal and gynecologic sepsis, rheumatism, unresolved pneumonia and lung abscess and tonsillitis; traumatic and infectious diseases of nervous system including psychosis; diseases connected with disordered trophic function of tissue, for example, duodenal and gastric ulcer, ozena and eczema. Am. Rev. Soviet Med., 1: 127 (Dec.) 1943.

SERUM, SPOTTED FEVER IMMUNE

Guinea Pigs—

Protection: Intracutaneously, 0.4 ml. unrefined immune rabbit serum protected guinea pigs against 0.1 ml. spotted fever virus injected in same area simultaneously or within 48 hours. Immunity was frequently but not necessarily established. Anigstein, J. Immunol., 48: 69 (Jan.) 1944.

SILVER NITRATE

Man—

Eye: One to 3% could be safely used to remove foreign bodies, especially those containing iron, from the cornea. Gillette, Arch. Ophth., 31: 129 (Feb.) 1944.

Uses: Closure of sinus of infected corns was aided with wet dressings and application of 95% phenol or 50% silver nitrate. For neurovascular corns, 50 to 100% silver nitrate was applied after X-ray therapy with three doses at ten day intervals of 800, 650, and 500 gammas, respectively. For mosaic wart, 40% salicylic acid daily for five to seven days, then silver nitrate 0.06 gm. to 0.06 ml. was applied to exposed rete every four to five days. Montgomery and Montgomery, J.A.M.A., 124: 756; 1944.

SILVER, COLLOIDAL

Man—

Tonsillitis: In peritonsillar abscess, pain and dysphagia were relieved by local injection of 0.5 to 1.5 ml. of colloidal silver at site of maximum swelling Sabourin, Clin. Med., 49: 190 (July) 1942.

SILVER OXIDE

Cows—

Chronic Mastitis. 15 to 20 ml. of 25 gm. silver oxide in 500 ml. petrolatum cleared 61.7% by a single injection Schalm, J. Am. Vet. M. A., 104: 78 (Feb.) 1944.

SILVER PICRATE

Cows—

Vaginitis: Insufflation into vagina of 5 gm. dose of 1% dispersion of silver picrate in kaolin, every other day for maximum of three treatments. Folger, J. Am. Vet. M. A., 101: 73 (Feb.) 1944.

SKIODAN

Man—

Roentgenography. 60 ml. for retrograde pyelography. Following ureteronephrectomy, a hystero-graphy was performed with 7 ml. of viscous solution. Huff and Boger, J. Urol., 54: 116 (Aug.) 1915.

Urography: 8 ml. of 10% solution into right kidney and 5 ml. into left kidney. A bilateral crossed renal ectopia was made after retrograde urography. Norfleet, J. Urol., 54: 10 (July) 1915.

SODIUM AZIDE

Mice—

Toxicity. 0.023 mgm./gm. killed two of 17 mice, 0.005 mgm./gm. per day for ten doses killed four of 15 Herrick and Emerson, J. Bact., 48: 331 (Sept.) 1944.

SODIUM BENZOATE

Man—

Fatality: 6 gm. was given orally for hippuric acid excretion test to patient with liver damage. Excruciating substernal pain, dyspnea, orthopnea, and sudden rise in blood pressure followed by shock, occurred four hours later and repetition of test after 48 hours brought similar results. Patient died from liver failure. Kinsey and Wright, J. Lab. & Clin. Med., 29: 188 (Feb.) 1944.

SODIUM BICARBONATE

Monkeys—

Renal Lesions: 1.0 gm. sulfathiazole per kg. for 28 days caused death to four of five animals from renal lesions. No deaths resulted, due to renal pH, when an equivalent dose of sodium bicarbonate was added. Clemenko, Barlow, and Wright, Arch. Path., 32: 889 (Dec.) 1912.

Man—

Diabetic Ketosis: Intravenously, 15 to 55 gm. raised carbon dioxide combining power of blood, no effect on blood sugar level, and no ketogenic action. Owens, Wright, and Brown, Ann. Int. Med., 68: 1066 (Dec.) 1911.

SODIUM BISULFITE

Rats—

Potentiation of Epinephrine Toxicity: 0.2% added to epinephrine increased toxicity to LD₅₀ of 1.0 mgm/kg., subcutaneously, and 0.4 mgm. per kg., intramuscularly. Doses up to 300 mgm/kg. were tolerated. Richards, Fed. Proc., 1: 71; 1942.

SODIUM BROMIDE

Rats—

Electric Epilepsy: 3 gm/kg. hypodermically, produced violent and exclusively tonic convulsions. Delay and Saulairac, Compt. rend. Soc. de biol., 138. 60 (Jan.) 1944.

Man—

Effects 2.6 gm. daily for one month was conducive to more frequent and restful sleep. Blood bromide varied up to 141 mgm/100 ml. (average 58 mgm/100 ml.). Moore, Trowbridge, and Gray, Dis. of Nervous System, 3: 220 (July) 1942.

Intoxication: Orally, 0.65 gm. three times a day produced concentration of approximately 100 mgm.% in 15 to 20 days; orally, 1.3 to 2 gm.

three times a day produced 253 mgm.% on 15th day. Treatment consisted of 9 to 12 gm. sodium chloride per day orally, plus intravenous fluids. Sedation by 16 to 24 ml. paraldehyde, orally or by nasal tube or by 10 ml. paraldehyde in 1 liter of 5% glucose in saline. Kay, Smith, and Johnson, J. M. A. Alabama, 13: 284 (Mar.) 1944.

SODIUM CACODYLATE

Cattle—

Anaplasmosis: 1.6 to 2.0 gm. per 45 kg., the dose was given intravenously as 0.3 gm./ml. in 5% dextrose solution. Philips et al., Vet. Med., 39: 190 (May) 1944.

SODIUM CHLORIDE

Dogs—

Burn Shock: Subcutaneously, physiologic saline at 40 mm. Hg pressure was made to lessen loss of plasma and electrolytes after healthy dogs were dipped into water of 99° C up to forelegs for 20 to 40 seconds. Survival time of animals increased. Berman, Peterson, and Butler, Surg., Gynec. & Obst., 78: 337 (Apr) 1944.

Man—

Bromide Intoxication: 1.3 to 3.9 gm. four times daily was given to eight patients with mental symptoms from bromine intoxication. Two of the patients were also given 0.6 to 1 liter saline intravenously. Kitching, Brit. M. J., I, 754 (June) 1942.

Heat: Orally, 1.3 gm. in 0.5 liter water administered copiously and glucose were effective for heat exhaustion. Vomiting patient was given 0.9% solution by intravenous drip. Prevention of heat exhaustion by drinking ample cool water containing 0.65 gm/0.5 liter, and additional sodium chloride in food to bring total daily intake to at least 31 gm. Morton, Tr. Roy. Soc. Trop. Med. & Hyg., 37: 317 (May) 1944.

Heat Fatigue Prevention: 0.65 gm. tablets, one to be taken with alternate glasses of water consumed. U. S. War Dept. Circular, 129 and 169; through Army Med. Bull., 114 (Jan) 1942.

Irradiation Sickness: 10 gm. daily and small radiation dosage for duration of treatment. Am. J. Roentgenol., 47: 56 (Jan.) 1942.

Requirement of unacclimatized men sweating 5 to 8 liters per day was not greater than 13 to 17 gm. per day, intake above this amount resulted in increased loss of salt and water in urine with no apparent advantage. Taylor et al., Am. J. Physiol., 140: 439 (Dec.) 1943.

SODIUM FUMARATE

Rabbits—

Toxicity: 0.5 gm/kg. was fatal to some. Repeated 0.5 gm. doses, totaling 3.0 gm. given in two weeks was without ill effects in some. Bodansky, Gold, and Zahn, J. Am. Pharm. A. (Scient. Ed.), 31: 1; 1942.

Man—

Laxative Effect: Orally, 5 to 30 gm. was effective within ten hours. Ibid.

SODIUM HEXAMETAPHOSPHATE

In Vitro—

Anticoagulant: Presence of 1:20 in rabbit blood and 1:100 in human blood prevented coagulation. Caspe and Hadjopoulos, Am. J. Pharm., 114: 175 (May) 1942.

Rabbits—

Effect: Injection of 1 ml. of 10% solution per kg. into marginal ear vein resulted in shock and marked prolongation of coagulation time of arterial blood. Ibid.

SODIUM HYPOCHLORITE

Bacteria—

Aerial Disinfection: 1% solution in concentration of 2.1 ml/1000 cubic feet of air killed bacteria emitted by sneezing. Bourdillon, Lidwell, and Lovelock, Brit. M. J., 1: 42; 1942.

SODIUM IODIDE

Mice (white)—

Histoplasmosis: Intraperitoneally, 1.8 mgm. every 24 hours begun 24 hours after infection was of no value. Levy, Am. J. Trop. Med., 25: 241 (May) 1945.

Man—

Expectorant Action: One to 2 gm., given intravenously, was excreted in bronchial tree from blood within 15 to 25 minutes. Tuft and Levin, Am. J. M. Sc., 203: 717 (May) 1942.

SODIUM LACTATE

Man—

Acidosis: Volume of 1/6 M sodium lactate required for a given case was: dose in ml. = (60—carbon dioxide combining power) × (0.8 body weight in pounds). Rupert, J. Urol., 47: 379 (Mar.) 1942.

Diabetic Acidosis: Subcutaneously or by venoclysis, 500 ml. of 0.166 M solution for patients under 15 years; 1000 ml. for adults. Supplementary doses were dependent upon chemical response of patient. Beardwood and Rousse, J.A.M.A., 117: 1701; 1941.

Acidosis in Newborn: 1/6 M solution (60 ml/kg.) was given subcutaneously. In severe cases, one third to one-half was given intravenously and the rest subcutaneously. Lawson and Venning, North Carolina M. J., 4: 510 (Dec.) 1943.

Acidosis in Premature Infants. Treated with 60 ml. 1/6 M solution per kg, one-third by vein and two-thirds subcutaneously. Subcutaneous route was more efficient than intravenous administration since 90% was excreted unmetabolized when given intravenously. McBryde and Branning, J. Pediat, 20: 549 (May) 1942.

Burn Shock Therapy: 1.75% (isotonic) solution, orally, administered at once and at 15 minute intervals to a total of seven to ten liters within 24 hours was effective in third degree burn Fox, J.A.M.A, 124: 207; 1944.

SODIUM LAURYL SULFATE

Man—

Duodenal Ulcer: 780 mgm per hour did not produce detectable lowering of peptic activity when administered with 90 ml. milk and cream to three patients. 780 mgm. per hour, given to five patients receiving diets low in lipids, resulted in temporary decrease in peptic activity. Kirsner and Wolff, Proc. Soc. Exper. Biol. & Med, 54: 11 (Oct) 1943.

SODIUM MORRHUATE

Man—

Varicose Veins: Injection of 2 to 5 ml 5% was repeated every few days in mild localized varicosities with negative "constriction tests." High ligation, division and retrograde injection with 8 ml. 5%, or 10 ml. were made if varicosities were very large in great saphenous varicosities with positive Trendelenburg constriction test. Clark, Canad. M. A. J., 50. 217 (Mar.) 1944.

SODIUM NITRITE

Rats—

Blood P
mgm. per
sive rats. Rath and Krantz, Proc Soc. Exper Biol & Med, 20: 410 June, 1942.

Man—

Choroidosis Centralis Serosa Therapy: 0.1 gm. was given intravenously. Duggan, Arch. Ophth., 27: 123; 1942.

Fatality: 2.3 gm. found in stomach contents. Death followed one hour after ingestion. Manley, Analyst, 70: 50 (Feb.) 1945.

Stomach: 0.06 gm. produced an average delay of 23.6% in gastric emptying time in seven subjects. Sleeth and Van Liere, Arch. internat. de pharmacodyn. et de therap., 65: 5 (Jan.) 1941.

SODIUM POTASSIUM BISMUTH TARTRATE (Sobita)

Man—

Yaws: 12 weekly intravenous injections were given. Average dose for clinical arrest was 0.14 gm. Sobita, 0.65 gm. was as effective as 0.45 gm. neoarsphenamine. de Wyt, J. Roy. Army M. Corps, 81: 255 (Dec.) 1943.

SODIUM PROPIONATE

Mice (white)—

Experimental Histoplasmosis: Intraperitoneally, 1.5 mgm. for ten days starting 24 hours after infection was unsuccessful. Levy, Am. J. Trop. Med., 25: 241 (May) 1945.

Man—

Fungus Infection: Topical application of 10% ointment or powder or 20% aqueous solution was effective for 90 patients. It was effective for tinea cruris, tinea pedis, otomycosis, thrush, tinea glabrosa, tinea capitis. There was no toxic reaction; only one of 90 developed contact dermatitis. Keeney and Broyles, Bull. Johns Hopkins Hosp., 73: 479 (Dec.) 1943.

SODIUM, RADIOACTIVE

Man—

Circulation Time. 50 to 300 micro-curies in 3 to 10 ml. normal saline gave arm to foot circulation time of 15 to 90 seconds (average 40 seconds) in 45 patients with peripheral vascular disease. Smith and Quimby, Surg., Gynec. & Obst., 79: 142 (Aug.) 1944.

Vaginal Absorption Radioactive sodium, given as 105 to 150 mgm. sodium chloride in 10 ml. solution readily passed into general circulation following instillation in traumatized vagina. Pommerenke and Hahn, Am. J. Obst. & Gynec., 46: 853 (Dec.) 1943.

SODIUM SALICYLATE

In Vitro—

Sedimentation Rate: 90 mgm/100 ml. fresh plasma and 25 to 30 mgm/100 ml. plasma kept at room temperature for 24 hours caused marked reduction in sedimentation rate of red blood cells. Homburger, Am. J. M. Sc., 210: 168 (Aug.) 1945.

Man—

Effect of Sodium Bicarbonate: Orally, 7.2 to 10 gm. per day given to four with rheumatic fever and two in good health. Equal doses of sodium bicarbonate definitely lowered serum salicylate level. Smull, Wégria, and Leland, J.A.M.A., 125: 1173; 1944.

Fatalities: 10 gm. per one liter isotonic salt solution daily for two days and then orally, 10 gm. for four days resulted in mental disturbance, hyperpyrexia, hyperpneic attacks, and death. Ashworth and McKensie, J.A.M.A., 126: 806; 1944.

A total of 26 gm. (0.7 gm/kg.) caused deep and labored respiration and death. Toxic encephalopathy observed at autopsy. Ryder, Shaver, and Ferris, New England J. Med., 232: 617 (May) 1945.

Blood Levels over 350 microgram/ml. were maintained in two children with 0.2 and 0.22 gm. respectively, every 24 hours. Fashena and Walker, Am. J. Dis. Child., 68: 369 (Dec.) 1944.

Intoxication. Child of nine years was given orally 6 gm. daily for four days, 8 gm. daily for four days, and later developed hyperpnea, enlargement of heart, nausea, vomiting, hypoprothrombinemia, acidosis, disorientation and coma. Treated with vitamin K—1 mgm. injected four times a day. Rapid recovery. Fashena and Walker, Am. J. Dis. Child., 68: 369 (Dec.) 1944.

Rheumatic Fever: 0.45 to 0.65 gm. divided throughout day was given with excess of sodium bicarbonate. In acute stages, most effective drugs were salicylates and aminopyrine. Salicylates were safer, but caused gastrointestinal irritation and in such cases aminopyrine was drug of choice. Swift et al., New York State J. Med., 42: 900 (May) 1942.

Plasma salicylate of at least 0.35 mgm/ml. required. Less than 0.20 mgm/ml. plasma level relieved symptoms without suppressing rheumatic inflammation. Intravenous drip of 10 gm. per one liter, 0.9% sodium chloride in four to six hours on first day, 20 gm. per two liters, saline in eight hours on second day, 10 gm. on third, if patient were symptom free, otherwise, 20 gm. Ten gm. were continued until seventh day, when oral administration of 1.6 gm. with 0.6 gm. sodium bicarbon-

ate, every four hours day and night were given until 30th day. Coburn, Bull. Johns Hopkins Hosp., 73: 435 (Dec.) 1943. Intravenously, 1.0 or 1.5% solution, beginning 33 hours after hospitalization reduced acute symptoms with minimum side reactions in 30 patients. Average of 13 daily injections were given. Temperature dropped to normal in four and a half days, and joint pains disappeared in two to eight days. Martin, U. S. Nav. M. Bull., 44: 1000 (May) 1945.

Orally, 10 to 13.3 gm. in combination with an equal amount of sodium bicarbonate had no greater benefit than daily dose of 0.2 gm. salicylates. Returned to normal in four weeks. Joint pains alleviated in one to two days with high dosage and three to four days with low. Blood levels were 35 mgm.% with 13.3 gm. daily and 27.0 mgm.% with 10 gm. daily. Keith and Ross, Canad. M. A. J., 52: 554 (June) 1945.

10 gm. per day intravenously, was followed by 10 to 16 gm., orally. Massive 10 gm. doses were more satisfactory than smaller doses. Salicylism occurred at 25 to 35 mgm./100 ml. blood levels, which was aborted by intravenous administration of one to two liters of normal saline with 0.6 gm. sodium bicarbonate orally, every four hours. Wright, Bull. New York Acad. Med., 21: 419 (Aug.) 1945.

SODIUM SELENITE

Mice—

Tumors: 0.02 mgm., intraperitoneally for nine injections caused regression in approximately one-fourth of animals. Turner, J. Nat. Cancer Inst., 4: 265 (Dec.) 1943.

Man—

Rheumatic Fever: Orally, 1.6 gm. was given with 0.65 gm. sodium bicarbonate twice a day for one week, four times a day for one week, and every four hours for the third week, and 2 gm. every four hours with 0.65 gm. sodium bicarbonate the fourth week. Prothrombin level was normal at 3.2 gm. daily, began increasing at 6.6 gm. daily, and was elevated at 10 gm. daily. Blood levels were 30 to 50 mgm.% on a 10 gm. dose daily, reaching zero in three to four days after discontinuance of treatment. Butt et al., J.A.M.A., 128: 1195; 1945.

SODIUM STIBOGLUCONATE

Hamsters (Syrian)—

Experimental Leishmaniasis: Subcutaneously, 250 to 500 mgm/kg. significantly reduced number of leishmania in spleen. Goodwin, Tr. Roy. Soc. Trop. Med. & Hyg., 38: 151 (Nov.) 1944.

SODIUM SUCCINATE

Rats—

Barbiturate Antagonist. Intramuscularly, 100 mgm/100 gm., 15 minutes prior to intraperitoneal administration of 8.5 mgm., pentobarbital sodium per 100 gm. protected 80% of treated animals from death; 47.5% of controls survived. Mean recovery time was 317 and 320.5 minutes, respectively. Pinschmidt, Ramsey, and Haag. *J. Pharmacol. & Exper. Therap.*, 83: 45 (Jan.) 1915.

Rabbits—

Barbiturate Antagonist: Slow intravenous injection of 1 gm/kg. shortened duration of anesthesia of intravenous application of 35 mgm. pentobarbital sodium per kg., but 2 mgm. picrotoxin per kg. intravenously was more effective. Two mgm. picrotoxin and 1 gm. sodium succinate per kg. was slightly more effective than picrotoxin alone. *Ibid.*

SODIUM SULFATE

Man—

Bacillary Dysentery: 7.8 gm. to acute cases on admission followed by 4.0 gm. for three doses every two hours, then 4.0 gm. every four hours for three to four days after which it was reduced to one morning dose. Many cases responded to rest and large fluid intake. Hone, Keogh, and Andrew, M. J. Australia, 1 631 (June) 1912.

SODIUM SULFATHIAZOLE SESQUIHYDRATE

Man—

Renal Function in Children Intravenously, 0.1 gm. in 10 ml. sterile distilled water caused 11.5 to 37.1% to be excreted in two hours in children without kidney pathology, and only 7.5 to 20.1% to be excreted within two hours by children with kidney pathology. Kato, *J. Pediat.*, 20: 576 (May) 1942.

SODIUM THIOCYANATE

Man—

Hypertension: 10 to 16 mgm/100 ml. blood levels with administration of sufficient amounts of drug reduced systolic and diastolic blood pressure an average of 40.5 and 19.8 mm. Hg. respectively, in ten patients. Beamish and Adamson, *Canad. M. A. J.*, 53: 236 (Sept.) 1915.

SODIUM THIOSULFATE

Man—

Gold Dermatitis: Gradually improved with three intravenous injections of 1 gm. doses. Spectrographic examination showed 0.5 microgram gold in skin and 0.15 microgram gold per gm. of blood. Ludy and Thomas, Arch. Dermat. & Syph., 49: 365 (May) 1944.

SOLUPYRIDINE

Mice—

Toxicity: LD₅₀ was 1.28 mgm/gm., intravenously; 2.68 mgm/gm., subcutaneously; and 7.5 mgm/gm., orally. Acute toxicity signs appeared within five minutes after intravenous injection and consisted of ataxia, severe convulsions of the clonic type and respiratory failure. Wien et al., J. Pharm. & Exper. Therap., 84: 203 (July) 1945.

Rabbits—

Blood Levels: Subcutaneously, 0.125 gm/kg. initially, followed by 0.75 gm/kg. at one and a half hour intervals maintained level at 15 mgm.%. Level fell to 5 mgm.% within four hours after last injection. Wien and Hampton, J. Pharmacol. & Exper. Therap., 84: 211 (July) 1945.

Cows—

Blood Level: Infusion into udders of 225 ml. of 4.5% solution produced a maximum of 14 mgm.% in one hour in blood. Ibid.

Man—

Blood Levels: Intravenously, 20 ml. of 20% solution gave values of 17.8, 10.2, 8.0, and 5.1 mgm.% free drug at half, one and a half, three, and six hours later. High blood level could be maintained by additional injections not more than six hours later, on oral administration of parent compound. Ibid.

Excretion: Intravenously, 20 ml. of 20% solution produced 40 to 70% elimination in 12 hours and urinary concentration from 240 to 1170 mgm.%. Less than 10% was acetylated. Ibid.

SOLUTHIAZOLE

Rabbits—

Blood Levels Subcutaneously, 0.125 gm/kg. initially, followed by 0.075 gm/kg. at one and a half hour intervals maintained level at 15 mgm.%. Level fell to 5 mgm.% within four hours after last injection. Wien and Hampton, J. Pharmacol. & Exper. Therap., 84: 211 (July) 1945.

Man—

Absorption: Intramuscularly, 5 ml. of 20% solution showed blood concentrations of 4.3, 4.2, 3.5, and 2.7 mgm.% free drug, half, one and a half, three, and six hours later, respectively. Intravenously, 20 ml. of 20% solution gave corresponding values of 14.5, 11.2, 8.7, and 6.0. This high level could be maintained by additional injection not more than six hours later, or by oral administration of parent agents. *Ibid.*

Excretion: Intramuscularly, 5 ml. of 20% solution or intravenously, 20 ml. of 20% solution gave 40 to 70% excretion in 12 hours and urinary concentration from 240 to 1,170 mgm.%. Less than 10% was acetylated. *Ibid.*

SOLUSTIBOSAN
(Stibanose)**Hamsters—**

Experimental Kala Azar. Arrest affected with single intravenous injection of 6 ml. of oil suspension (324 mgm. antimony) per kg. as against eight injections of aqueous solution of 500 mgm/kg. (1080 mgm antimony). Kikuth and Schmidt, *Deutsche tropenmed. Ztschr.*, 47: 247 (May) 1943; *Trop. Dis. Bull.*, 41: 194 (Mar) 1944.

Man—

Kala Azar (Ramos): Five intramuscular injections of 1 ml/kg. (54 mgm. pentavalent antimony per ml of oil) were given at two day intervals to children. Response was rapid in 90%. Concentrated drug (100 mgm. pentavalent antimony per ml.) was given in 0.4 ml/kg. doses in ten injections in five days. *Ibid.*

Intramuscularly, in gluteal region in total dose of 0.06 ml/kg. (100 mgm. pentavalent antimony per ml) produced marked increase in weight, reduction in splenomegaly and return to normal blood picture in children. Doses to body weight tabulated Lozano, *Med Colonial, Madrid*, 6: 372 (June) 1943, through *Trop Dis Bull.*, 41: 195 (Mar.) 1944.

24 cases were treated with 60 ml to 162 ml Chung, Wang, and Lee, *Chinese M. J.*, 62: 17; 1944.

SORBITOL**Monkeys (Rhesus)—**

Liver Glycogen. 8 gm/kg orally raised average liver glycogen of 0.28% (after 24 hour fasting) to 0.72% in three hours. Ellis and Krantz, *J. Biol. Chem.*, 141: 147; 1941.

Chronic Toxicity: 3 gm daily for three months showed no histopathologic or toxicologic indication. *Ibid.*

Man—

Pharmacology: 10 gm. daily for one month produced no significant changes in non-protein nitrogen, carbon dioxide combining power of blood, or red blood cell count, and no damage to kidney. Laxative threshold was 20 to 30 gm. of sorbitol syrup or 50 gm. of crystalline sorbitol. 50 gm. increased respiratory quotient above basal level but had no effect on blood sugar level. Ibid.

STAPHYLOCOCCUS BIOLOGICS

Man—

Staphylococcic Ocular Inflammation: 10,000 units antitoxin injected daily improved temporarily. Ascending doses at weekly intervals of vaccine beginning with 0.1 ml. each dose increased with 0.1 ml. until 1.0 ml. was given. Allen, J. Lancet, 62: 207 (June) 1942.

Hematogenous Osteomyelitis Juvenilis: Therapy consisted of bed rest; 60,000 to 100,000 units of a potent antistaphylococcal serum daily, intravenous or oral sulfathiazole, maintenance of water balance, blood volume, plasma volume, and blood cellular volume. Gage, Surg., Gynec. & Obst., 76: 123 (Jan.) 1943.

STAPHYLOCOCCUS ENTEROTOXIN

Man—

Antigenic Property: A few subcutaneous injections, totaling 0.2 to 0.5 ml. of filtrate containing staphylococcus enterotoxin enabled five patients to resist twice the dose of enterotoxin which had previously made them ill. Canad. Pub. Health J., 35: 92 (Feb.) 1944.

STILBAMIDINE

(4,4'-stilbenecarboxamidine)

Monkeys—

Experimental Malaria: 16 of 20 survived 0.001 to 0.005 gm per kg. One of eight given 0.002 gm. or more per kg. relapsed, but none given 0.003 to 0.005 gm. per kg. did. Das Gupta and Siddons, Indian M. Gaz., 79: 527 (Nov.) 1944; through J. Trop. Med. & Hyg., 48: 32; 1945.

Man—

Bilharziasis Therapy. 2.0 to 2.2 gm. in 15 injections, consisting of one to two courses cured two of nine cases. Stephenson, Tr. Roy. Soc. Trop. Med. & Hyg., 38: 306 (Mar.) 1945.

Excretion Nine injections of 50 mgm. each were given on alternate days to two patients. 41% and 53%, respectively, of total amount of drug

injected were excreted in urine by fourth day after last injection. Plasma levels were 0.8 and 0.6 mgm % respectively, 15 to 20 minutes after ninth injection Kirk and Henry, Ann. Trop. Med., 38: 99 (Sept.) 1944.

Leishmaniasis in two children Relapse after 1.17 gm. was treated with 0.54 gm. urea stilbamine followed by 3.75 gm. stilbamidine. Other child received 5.5 gm. over six months. Complete arrest. Susskind and Roth, Ann. Trop. Med., 37: 158 (Dec.) 1943.

STILBESTROL MONOMETHYL ETHER

(Methyl Stilbestrol)

Rabbits—

Endometrium: 105 to 210 gammas failed to inhibit endometrial response to progesterone stimulation in inseminated, ovariectomized animals. Werthesen and Gargill, Endocrinology, 37: 15 (July) 1945.

Man—

Menopause Therapy: Orally, 0.5 to 1.0 mgm. daily or 5 to 25 mgm. injected monthly. 89% responded favorably Elden, J. Clin Endocrinol., 2: 287 (May) 1942.

Menopause, Dysmenorrhea Orally, 0.1 mgm every other day to 2.5 mgm. daily for menopause cases. Orally, as high as 30 mgm. was given daily for dysmenorrhea case Buxton and Sullivan, J. Clin Endocrinol., 2: 290 (May) 1942.

STOMACH

Dogs—

Experimental Polycythemia: Orally, 10 gm. given daily, markedly reduced red blood cell counts in polycythemic dogs. Davis, Proc. Soc. Exper. Biol. & Med., 54: 193 (Nov.) 1913.

Man—

Infantile Pellagra 10 gm plus 10 ml. of 0.1 N hydrochloric acid daily for five days brought recovery within one week in six patients Gillman and Gillman, J.A.M.A., 129: 12; 1945.

Orally, 10 gm. with 5 ml. of 0.1 N hydrochloric acid daily, for five days effected complete recovery in ten to 21 days in nine cases. Gillman and Gillman, Arch. Int. Med., 76: 63 (Aug.) 1915.

STREPTOMYCIN

In Vitro—

Estimation in Body Fluid: 0.5 ml. amounts of modified broth in Wassermann tubes and serial dilutions by halves were made. Standard was

10 microgram of streptomycin salt per ml. Serial dilution: 1.5 ml. of 1:100 dilution of test organism in broth added to tubes and incubated overnight. End point was last tube without growth. Price, Nielsen, and Welch, Science, 103: 56; 1946.

Agar test plates prepared from modified F. D. A. nutrient agar, seeded with 10^{-5} dilution of a six hour culture in F. D. A. broth of *Staphylococcus aureus* S. M. Streptomycin was measured by a diameter in millimeter of zone of inhibition produced around beveled glass cylinders set in seeded agar and containing suitable dilution of sample. Stebbins and Robinson, Proc. Soc. Exper. Biol. & Med., 59: 255 (June) 1945.

Tetanus Toxin: 10 mgm. did not affect toxicity of toxin. Neter, J. Infect. Dis., 76: 20 (Jan.-Feb.) 1945.

Chicks—

Experimental Malaria: Intramuscularly, every three hours, 400,000 units per kg. per day was slightly effective. Seeler, Malanga, and Pierson, Proc. Soc. Exper. Biol. & Med., 59: 291 (June) 1945.

Mice—

Experimental Spirochetosis: Injections given five times daily to total of 1,000 units daily in saline, over four days. 15 of 50 treated and one of untreated were free of spirochetes in 24 hours. Relapses were five and 34, and mortality rates 8% and 20% for treated and untreated groups, respectively. Heilman, Proc. Staff Meet., Mayo Clin., 20: 169 (May) 1945.

Friedländer Infection: 185 to 500 units per day, subcutaneously, in 37 to 250 units per 0.05 ml. of 3% beeswax, given two to three times a day, protected 62 of 69 mice infected with 1000 to 10,000 times lethal dose of *Klebsiella pneumoniae*. Heilman, Proc. Staff Meet., Mayo Clin., 20: 33 (Feb.) 1945.

Prophylaxis. 190 to 380 units prevented infection with *Salmonella schottmülleri*, *Pseudomonas aeruginosa*. 35 mgm/20 gm. was tolerated; LD₁₀₀ was 135 mgm/20 gm. Jones et al., Science, 100: 103; 1944.

Experimental Tuberculosis: Intramuscularly, 5000 units daily for 90 days was superior to results obtained with 0.5 gm/kg. promin given orally. Smith and McClosky, Pub. Health J., 60: 1129 (Sept.) 1945.

Hamsters—

Experimental Spirochetosis: Subcutaneously, daily total of 250 units was incapable of protecting 12 animals (given with penicillin). Heilman, Proc. Staff Meet., Mayo Clin., 20: 169 (May) 1945.

Experimental Weil's Disease: All survived with daily total of 1000 units in saline four times a day. Treatment was started 17 hours after

inoculation and continued for ten days. 100% mortality for controls. Ibid.

Guinea Pigs—

Experimental Tuberculosis: 3000 to 6000 units daily produced an index of infection of 5.8 as against 67.0 in untreated controls. Feldman and Hinshaw, Proc. Staff Meet., Mayo Clin., 19: 593 (Dec.) 1944.

Rabbits—

Experimental Syphilis. Intramuscular injections of penicillin G, commencing within three days of infection, were made every four hours for four days. Streptomycin potencies were 158 units per mgm. to 229 units per mgm. Smallest total amount that cured any of animals was 79,000 units per kg. (375 mgm. per kg.) in one experiment and 187,000 units per kg. (817 mgm. per kg.) in another. A similar effect was obtained with 147 units per kg. (0.088 mgm. per kg.) of crystalline penicillin G; therefore, penicillin G was 3000 times as effective. Dunham and Rake, Science, 103: 365; 1946.

Dogs—

Absorption and Excretion. Antibiotic was given intravenously, intramuscularly and orally to 14 dogs of both sexes in amounts of 100,000 to 420,000 units. High blood levels were obtained following parenteral administration, and 23 to 65% was excreted in urine. Maintenance of plasma levels was no better with intramuscular than with intravenous injection. Could not be detected in blood during 24 hours after oral administration, but 3.9% was recovered in urine. Graham, Vander Brook, and Kuizenga, Science, 103: 364 (Mar 22) 1946.

Man—

Blood Levels: 600,000 units in 100 ml. tap water, taken orally could not be detected in blood. Intravenously, 200,000 units gave maximum level in five minutes, and one unit per ml. after eight hours. Intravenously, a single dose of 600,000 units produced a level of three units per ml. of serum 11 hours later. 200,000 or 300,000 unit doses given parenterally in two to 8.5 hours produced a trace to one unit per ml. in cerebrospinal fluid. Anderson and Jewell, New England J. Med., 233: 485 (Oct.) 1945.

Excretion: 57% of amount injected was excreted in urine in 24 hours. Greatest amount was excreted during first four hours and one-fifth to one-third the injected dose was excreted during fourth to 12th hour. Ibid.

Clinical Uses: Bacteremia due to *Escherichia coli*, *Aerobacter aerogenes*, *Pseudomonas aeruginosa*, *Proteus ammoniae*, salmonella or brucella was successfully treated in six of eight cases with intravenous or intramuscular administrations of 1,400,000 to 43,000,000 "S" units. Urinary

tract infection was treated with 1,000,000 to 2,000,000 units per day, intramuscularly. Pulmonary suppurative disease became free of causative organisms after intramuscular administration or nebulization of 1,120,000 to 30,000,000 units. Herrell and Nichols, Proc. Staff Meet., Mayo Clin., 20: 449 (Nov.) 1945.

Serum Levels: Intravenously, 200 mgm. produced immediate levels of 32 gammas/ml., which fell rapidly to eight gammas in two hours and to one to two gammas in 12 hours. Intramuscularly, 200 mgm. produced a peak level of 16 gammas/ml. in one hour, but appreciable amounts were detected after 12 hours. Waksman and Schatz, J. Am. Pharm. A. (Scient. Ed.), 34: 273 (Nov.) 1945.

Tissue Levels: Intravenously and intramuscularly, two million units were given in 24 hours, blood and blood serum levels were respectively, five to seven and 13 to 14 units per ml.; 29% urine recovery followed intramuscular administration and 68% urine and 2% fecal recovery after intravenous injection. Orally, four million units daily produced no demonstrable blood level, a 1% urine recovery and approximately 64% fecal content of streptomycin. Elias and Durso, Science, 101: 589; 1945.

Toxicity: Nine patients, 15 to 61 years, received total of 1,850,000 units over 48 hours to 72,250,000 units in 56 days; six received intramuscularly, at three or four hour intervals, two by continuous intravenous infusion and one by continuous hypodermoclysis. One patient also received 40,000,000 units orally over 11 day period in addition to that administered parenterally. Before and after administration of streptomycin, urea clearance, bromsulfalein retention, cephalin cholesterol flocculation and complete blood counts, including differential leukocyte counts showed no evidence of serious toxicity. Hettig and Adcock, Science, 103: 355; 1946.

Typhoid: One patient received ten million units intramuscularly in doses of 125,000 units every three hours; begun on 24th day of illness and showed improvement in 36 to 48 hours. Blood level maintained at five units per ml.; 13 to 56% of total daily dose excreted in urine. Varied doses were given. Recovery in three of five patients. Reimann, Elias, and Price, J.A.M.A., 128: 175; 1945.

Urinary Concentration: 1,330 units per ml. at first determination and 1,131 to 1,175 units per ml. two to three months later in a 24 hour urine specimen from a patient given two million units per day orally, for several weeks. Helmholz, Proc. Staff Meet., Mayo Clin., 20: 357 (Oct.) 1945.

STREPTOTHRYCIN**In Vitro—**

Antifungal Action. 50 mgm/5 ml culture of *C. albicans* was effective with continued contact, only trace of growth being visible after seven days. Reilly, Schatz and Waksman, *J. Bact.*, 49: 585 (June) 1945.

Chick Embryos—

Brucella abortus completely destroyed with simultaneous administration of 10 mgm. crude streptothrycin in living chick embryo. Metzger, Waksman, and Pugh, *Proc. Soc. Exper. Biol. & Med.*, 51: 251 (Nov.) 1942.

Mice—

Toxicity: 60,000 units per kg crude streptothrycin, intravenously, killed two of ten in five days. Same dose orally, or subcutaneously was non-toxic. 25,000 units per kg. orally, while non-toxic, caused 80% deaths when given by intravenous route and 100% when given subcutaneously. 10% mortality resulted by 50,000 units per kg. orally, and 100% mortalities by intravenous or subcutaneous routes Robinson et al, *Science*, 99: 540 (June 30) 1944.

Rabbits—

Experimental Wound (Beta hemolytic streptococcus) One mgm. of powder reduced number of organisms in five of nine experiments as compared to one of 16 for 100 mgm of powdered sulfathiazole. Neter, Hubbard, and Lambert, *Am. J. Surg.*, 69: 204 (Aug) 1945

Man—

Ringworm Infection: Ointment containing 5000 units, plus 0.2 ml. triethanolamine, and 30 ml greaseless base was fungistatic but not fungicidal. Greenbaum, *J.A.M.A.*, 129: 1045, 1945.

STROPHANTHIN**Man—**

Effect on Blood Pressure. Intravenously, in 0.25 and 0.5 mgm. doses to healthy persons produced an initial bradycardia and significant decrease in systolic blood pressure, followed by increase in blood pressure reaching highest value 60 seconds after completion of injection. After 0.25 mgm., blood pressure increase was slight and lasted at most for four to five minutes. After 0.5 mgm., initial increase was more acute, intensive but not protracted. Respiratory frequency decreased constantly, immediately after completion of injection and reached minimum two to three minutes later. Busse and Struppler, *Arch. f. exper. Path. u. Pharmacol.*, 202: 132 (Aug) 1943.

STRYCHNINE

Man—

Action: Subcutaneously, 3 mgm. increased volume and hydrochloric acid content of gastric juice in four with normal gastric acidity, but changes did not occur in four with achlorhydria. Strong gastric contraction lasting 20 to 45 minutes occurred in eight given strychnine during period of quiescence. Subcutaneously, 3 mgm. of hydrochloride three times a day for three to four weeks shortened stomach emptying time of test meal in four of seven. Hydrochloric acid in gastric juice was reduced in one hyperchlorhydria patient and in one achlorhydric, stomach hydrochloric acid appeared. Anderson, Brit. M. J., I: 360 (Mar.) 1944.

STYRENE

Man—

Toxicity: Styrene fumes in concentration of 500 parts per million or less developed nasal, throat and lung irritation, lassitude, fatigue, and in some cases coughing, mild conjunctivitis and roughened dry skin. Pathologic changes, chronic toxicity or cumulative toxicity were not found in any of the men exposed to styrene and observed at least one year. Wilson, J.A.M.A., 124: 701; 1944.

SUBTILIN

Mice—

Acute Toxicity: LD₅₀'s were 60 ± 3 mgm/kg. of 1% solution given intravenously; and 670 ± 30 mgm/kg. given subcutaneously; intragastically, 5 gm/kg. was lethal. Anderson et al., Science, 103: 419 (Apr. 5) 1946.

SUCCINATE COMPOUND

Man—

Rheumatic Fever: 4.0 to 5.3 gm. of calcium double salt of benzoic acid and succinic acid benzyl ester, and 200 mgm. ascorbic acid daily for 27 days was far more effective than sodium salicylate. Carditis and electrocardiographic abnormalities developed in only 19% and 9%, respectively. Gubner and Szucs, New England J. Med., 233: 652 (Nov.) 1945.

SUCCINYL SULFATHIAZOLE

Mice—

Toxicity: LD₅₀ was 5.7 gm/kg., intraperitoneally given in olive oil suspension, and 7.5 gm. of sodium salt per kg. in aqueous solution, given by same route. Orally, 40 gm/kg. produced no toxic effects and very

slight absorption, and blood concentration was 4.2 mgm.% two hours later. Welch, Mattis, and Latven, *J. Pharmacol. & Exper. Therap.*, 75: 231 (July) 1942.

Rats—

Chronic Toxicity: There was no toxic effect after being fed for 33 days on chow containing 5% of drug. Blood concentration was 4.6 mgm.% of drug and 1.4 mgm.% of sulfathiazole. *Ibid.*

Biotin Deficiency: Basal diet containing egg white and 0.75% succinyl sulfathiazole plus beef liver, containing 2.4 micrograms of biotin and 31 micrograms of folic acid produced typical signs of biotin deficiency after 26 days. Emerson and Wurtz, *Proc. Soc. Exper. Biol. & Med.*, 59: 297 (June) 1945.

Monkeys—

Dosage and Concentration. Orally, 0.5 to 5.0 gm. sodium salt per kg. per day was given without toxic effects. Maximum blood concentration was 1.3 mgm.% sulfathiazole and 5.3 mgm.% succinyl-sulfathiazole. Parenteral injections of 1.0 gm. of sodium salt per kg. per day were given in 25% solution by various routes for ten days. Blood levels were 4.8 mgm.% sulfathiazole and 170 mgm.% succinyl sulfathiazole, and maximum urine concentration was 12.1 gm.%. Mattis and Welch, *Federation Proc.*, 1: 159; 1942.

Toxicity: Oral doses up to 5 gm./kg. per day of sodium salt, given every four hours by stomach tube for 30 days, showed no reaction of toxicity. Average blood concentration was 3.0 mgm.% of drug and 0.8 mgm.% of sulfathiazole and less than 4% was excreted by kidneys. Neutral, 25% solutions of sodium salt caused venous sclerosis on intravenous injection and local discomfort and hemorrhage after subcutaneous injections. No histopathologic changes resulted at 1.0 gm. of sodium salt per kg. per day for ten days to monkeys with kidneys removed. 12 gm./100 ml. were found in urine and crystals increased as pH declined. *Ibid.*

SULFACETAMIDE

(N-acetyl p-aminobenzenesulfonamide)

Mice—

Toxicity: Oral LD_{50} was 16.5 gm./kg. Fisher and Hoag, *J. Urol.*, 47: 183; 1912.

Rats (albino)—

Pharmacology: Average lethal dose was 7.6 gm./kg. Blood levels: 400 mgm./100 ml. survived by all animals, and 700 to 850 mgm.% was fatal.

Intraperitoneally, 0.6 gm. sulfacetamide sodium per kg. for nine weeks showed gain in weight and normal urinary flow. Lehr, J. Urol., 54: 87 (July) 1945.

Dogs—

Toxicity: LD₅₀ was 8 gm/kg., orally. 0.4 gm/kg., daily for 11 weeks was tolerated, but 1.0 gm/kg., daily resulted in death from renal impairment. Fisher and Hoag, J. Urol., 47: 183; 1942.

Man—

Antibacterial Action: 50 to 100 mgm/100 ml. human urine had antibacterial action equal for sulfathiazole and sulfacetamide. Lehr, J. Urol., 54: 87 (July) 1945.

SULFADIAZINE

Mice—

Hemolytic Anemia occurred at concentration of 33 mgm/100 ml. blood. Latven and Welch, J. Pharmacol. & Exper. Therap., 81: 301 (July) 1944.

Toxicity: Oral lethal dose was greater than 34 gm/kg. Intraperitoneal LD₅₀ was 3.8 gm/kg. Sodium salt was less toxic than sodium salts of others. In chronic toxicity, there was decreased food consumption and inhibition of growth with weight loss. No pathologic lesions observed at autopsy. Fine crystals deposited in kidney tubules. Powell and Chen, J. Indiana M. A., 34: 602 (Nov.) 1941.

Cats—

Intracranial Absorption: 65 to 120 mgm. given in cerebral wounds. Greatest speed of intracranial absorption was with sulfanilamide, then sulfathiazole, sulfadiazine and sulfapyridine. Hurteau, Canad. M. A. J., 46: 15 (Jan.) 1942.

Dogs—

Absorption Rate: Intraperitoneally, 100 mgm/kg. was given, Average blood concentrations during first seven hours were: 1.96, 3.0, 3.64, 3.5, 3.32, and 3.23 mgm/100 ml., respectively, and 2.4 mgm/100 ml. after 24 hours. For each succeeding 24 hours, values were: 1.5, 0.72, 0.6, 0.5, and 0.39 mgm/100 ml. Ambrose, Fed. Proc., 1: Part II-141; 1942.

Man—

Absorption Rate: 5 gm. placed in peritoneal cavity of four patients. Blood concentrations were: 3.17 mgm/100 ml. in 1.08 hours; 3.83 mgm. per 100 ml. in two hours; 2.15 mgm/100 ml. in three hours; and 1.93

mgm/100 ml. in six hours. Ambrose and Griswold, Fed. Proc., 1: Part II-142; 1942.

Anuria: 7 gm. in 24 hours caused fatal anuria in a patient. Baron, Kentucky M. J., 43: 227 (Sept.) 1915.

Sixth reported case in 25 year old woman with rheumatic heart disease. Two gm. was given twice within first two hours, then 1.0 gm. every four hours for five days. Blood level was 22.4 mgm/100 ml. Treated by ureteral catheterization with warm saline irrigation of kidney pelvis. Louria and Solomon, J.A.M.A., 120: 1354, 1912.

Blood Levels: At end of four hours, a single oral dose of 2 gm. gave 2.0 to 3.5 mgm. free drug per 100 ml., with 3 gm., 2.5 to 4.0 mgm. per 100 ml.; and with 5 gm., 3.6 to 5.5 mgm. per 100 ml. Retention enema containing 5 gm. never gave values above 1.0 mgm per 100 ml. Injection of 5 gm. sodium sulfadiazine in 50 ml. distilled water gave 16 to 21 mgm. per 100 ml. value in ten to 30 minutes. Intravenously, 500 to 1000 ml. of 0.5 to 1.0% solution of sodium salt, at rate of 2.5 to 3.0 ml. per minute gave rapid attainment and maintenance of high blood levels. Subcutaneously, 5 gm. sodium salt in 1000 ml. of physiologic saline in two hours gave from 7.5 to 8.2 mgm. per 100 ml. values in six hours. Ratish, Shackman, and Bullowa, New England J. Med., 226: 596 (Apr.) 1912. 5.0 to 25 gm. drug was sprinkled in peritoneal cavity at operation in six male patients. Blood level of 3.5 mgm.% or more was obtained for 48 hours after 10 gm., for 84 hours after 20 gm., for 96 hours after 25 gm. Ryan et al., J.A.M.A., 119: 481 (June) 1912.

Cholesterol Level: 2 gm. initially, then 1 gm. every six hours for four days increased average level from 151 to 214 in six children with pneumonia. Stoesser, Proc. Soc. Exper. Biol. & Med., 55: 278 (Apr.) 1911.

Gastric Juice. Highest concentration reached 15 to 15 minutes after intravenous injection of 5 gm. of sodium salt which gave gastric juice range of 4 to 21 mgm.%. Shapiro et al., Gastroenterology, 3: 39 (July) 1914.

Renal Complications: Hematuria in seven, given 5 gm. in one day to 72 gm. in 11 days. Blood level at onset of hematuria varied from 5.6 to 10 mgm. per 100 ml. Wright and Kinsey, J.A.M.A., 120: 1351 (Dec.) 1912.

Sensitivity was produced by 9 gm. given in 0.75 gm. doses at four hour intervals. Koteen, J.A.M.A., 126: 833, 1914.

Tolerance: 1 gm. daily was given for a prolonged period. Only 34 toxic reactions occurred out of 9,000 men treated. Warren, J. Indiana M. A., 37: 417 (Sept.) 1911.

SULFADIAZINE SODIUM**Dogs—**

Intracranial Implantation: 10 to 66 mgm/kg. applied locally led to no convulsions. Pilcher, Angelucci and Meacham, J.A.M.A., 119: 927; 1942.

Man—

Agranulocytosis: Intravenously, 5 gm. daily for 11 days, was followed by 2 gm. orally a day for seven days. Further intravenous dose of 2.5 gm. resulted in jaundice, agranulocytosis and finally death. Ziegler, Patterson, and Johnson, New England J. Med., 233: 59 (July) 1945.

SULFAGUANIDINE**Cats—**

Excretion: 3 gm. implanted subcutaneously and animals sacrificed 24 hours later. Average concentrations in mgm. per 100 ml. of free and of total sulfaguanidine respectively were: contents of colon 17 and 20; contents of ileum, 17 and 21; bile, 8.7 and 9.8; liver, 9.0 and 10.2; skeletal muscle, 8.3 and 9.0; kidney, 17 and 21; urine, 1180 and 2150; spleen, 9.0 and 10.2; blood six hours after implantation, 8.0 and 10.3; after death 24 hours after implantation, 11.0 and 12.8. Hawking, Lancet, 242: 704 (June) 1942.

Swine—

Pharmacology: Safe dose was 1 gm/10 kg. given twice daily for five days. Peak of blood concentration was 2.2 mgm.% free and 3.6 mgm.% total on fifth day, and declined to a trace on eighth day. Single dose blood concentration peak was 1.0 mgm.% free and 1.5 mgm.% total six to eight hours later. Peak of fecal concentration was 590 mgm.% on sixth day. Toxic dose was 5 gm/kg. given twice daily for five days. Pathologic lesion from lethal dose was a tubular nephritis. Cameron and McOmie, Vet. Med., 36: 612 (Dec.) 1941.

Man—

Pharmacology: 3 gm. single dose provided maximum blood concentration in four hours, and maximum stool concentration on second or third day. Average excretion was 30 to 66%. Stool specimens contained over 1000 mgm.% and had decreased colon organism counts. 29 to 40% excreted, when 3 gm. was given every eight hours for six to 14 days. Beling and Abel, J. M. Soc. New Jersey, 38: 629 (Dec.) 1941.

Toxicity: Febrile reaction, headache, backache, malaise and nausea occurred in 11.5% of 181 men on a course of 3.5 gm. thrice daily. Bunting et al., J.A.M.A., 125: 773; 1944.

SULFAMERAZINE

Mice—

Hemolytic Anemia produced by concentration of 31.0 mgm/100ml. blood. Latven and Welch, J. Pharmacol. & Exper. Therap., 81: 301 (July) 1944.

Man—

Plasma Concentration (of free drug): 15.4 mgm., 12.7 mgm., and 10.9 mgm/100 ml. maintained by patients given 1 gm. every four, six, and eight hours respectively, after an initial 3 gm. dose. Toxic reactions were dermatitis, leukopenia, fever, hematuria, nausea, vomiting and thrombocytopenia observed in 38 of 400 cases. Flippin, Rheinhold, and Gester, M. Clin. North America, 27: 1447 (Nov) 1943.

Plasma Binding Power With 10 mgm/100 ml. drug level and protein concentration of 7 gm/100 ml., binding values were 84% for sulfamerazine and sulfamethazine as compared to 56% for sulfadiazine. Gilligan, J. Pharmacol. & Exper. Therap., 79: 320 (Dec.) 1943.

SULFAMETHAZINE

(2-sulfanilamide-4,6-dimethylpyrimidine)

Man—

Absorption, Distribution, Excretion Orally, 2 to 4 gm. followed by 1.0 gm. every four to six hours produced levels of 1.0 to 23.0 mgm/100 ml. of free drug in serum; an average acetylation of 38.3%. Urinary excretion after a 3 gm. oral dose to 13 patients varied from 17.1 to 55% (average 40.1%) in 12 hours and after 24 hours an average of 71.8% was excreted. Rapidly diffused into pleural, ascitic and cerebrospinal fluid and into red blood cells. Clark, Murphy, and Flippin, J. Lab. & Clin. Med., 28: 1828 (Dec.) 1943.

Blood Levels: 4 gm. followed by 1.5 gm. every four hours gave levels ranging from 2.9 to 13.9 mgm. free drug per 100 ml. Levels varied from day to day, as much as 16 mgm/100 ml. Dowling, M. Ann. District of Columbia, 12: 468 (Dec.) 1943.

SULFANILAMIDE

In Vitro—

Blood: 0.1 gm. added to 5 ml. whole blood and tube inverted at once. Coagulation occurred in seven minutes and serum appeared in 60 minutes, and clot completely retracted in three hours. Pelner, J.A.M.A., 125: 178; 1944.

Dogs—

Inhalation Concentration: Maximum blood concentration of 2.3 and 2.4 mgm/100 ml. respectively, in two dogs and 33.2, 33.2, and 12.2 mgm. per 100 ml. for three dogs after intratracheal dose. Urinary drug level was 1,660 mgm/100 ml. in one dog. Romence and Harkins, Proc. Soc. Exper. Biol. & Med., 54: 8 (Oct.) 1943.

Liver Damage: 4 gm. of powdered drug given three times per week with food for two days to 40 months depressed gastric acidity, related to degree of liver damage. Four animals survived two, 22, 29, and 40 months, respectively, and seven others died within two to 14 days. Streicher, Am. J. Digest. Dis. & Nutrition, 12: 267 (Aug.) 1915.

Toxicity: 0.1 to 0.2 gm/kg. did not affect external behavior, but 0.5 to 1.2 gm/kg. caused ataxia, incoordination, and generally depressed conditional reflexes. Gantt and Marshall, Bull. Johns Hopkins Hosp., 77: 104 (Aug.) 1945.

Man—

Absorption: Single dose of 5.8 gm. was placed in rectum of 17 patients and in vagina of 15 patients. Blood studies six hours later indicated highest concentration in 24 hours in rectal cases and within six hours after vaginal application. Absorption uneven; levels after rectal administration were twice as high as vaginal application. Carrington et al., Surg. Gynec. & Obst., 78: 333 (Mar.) 1944.

Absorption from Pleural Cavity: Two to 15 gm. dose produced 200 mgm. per 100 ml. concentration in pleural fluid during first 24 hours. Burford and Graham, J. Thoracic Surg., 11: 203; 1941.

Percutaneous Application: Single dose as high as 16 gm. was used without blood concentration exceeding 4 mgm.%. Blood concentration was highest at first hour after administration and dropped rapidly in four hours, being absent in 24 hours. Of 14 cases, four had cyanosis, and nausea in one. Zondek, Bromberg, and Shapiro, Proc. Soc. Exper. Biol. & Med., 50: 116 (May) 1942.

Secretion in Milk: 1.66 gm. was given daily to ten patients in puerperal stage. Breast milk concentration was 0.65 to 1.99 mgm. free drug per 100 ml. Excretion in nursing infant was 0.4 to 3.3 mgm/100 ml. Maximum amount ingested by infant would be 38.8 mgm, and therapeutic dose for infant was 146 mgm. daily. Hepburn, Paxson, and Rogers, Arch. Pediat., 59: 413 (July) 1942.

2-SULFANILAMIDO-5-CARBOXYTHIAZOLE**Mice—**

Acute Toxicity: LD₅₀, orally, 8.0 gm/kg. intraperitoneally, 5.0 to 6.0 gm/kg.; subcutaneously, 8.0 gm/kg. Chronic toxicity was comparable with succinyl sulfathiazole. Winck, *Science*, 103: 719 (June 21) 1916.

Man—

Effect: Less than 1.0 mgm % was blood level when 0.25 gm/kg. per day was given orally for five days. Three to 11% of orally administered drug was excreted in urine, average, 6.1% 0.25 gm. initially, followed in four hours by 0.25 gm/kg. daily in six divided doses at four hour intervals showed less than 1,000 coli organisms per gm. of feces within 48 hours. *Ibid.*

SULFAPYRAZINE**Mice—**

Toxicity: 0.5, 1.0, 2.0, or 4.0 gm/kg. for ten days showed no signs of toxicity. Blood concentration was 38 mgm % Robinson, Siegel, and Graessle, *J. Pharmacol. & Exper. Therap.*, 79: 354 (Dec.) 1913.

Mice, Rats, Dogs—

Toxicity: 10 gm/kg. single oral dose was not toxic. *Ibid.*

SULFAPYRIDINE**Mice—**

Hemolytic Anemia: Occurred at concentration of 2.8 mgm/100 ml. blood. Latven and Welch, *J. Pharmacol. & Exper. Therap.*, 81: 301 (July) 1914.

Monkeys—

Toxicity: 0.5 gm/kg. was given in milk suspension by stomach tube. Death occurred at 13, 14, and 21 days after hematuria and anorexia. Post-mortem examination revealed urolithiasis, degenerative changes of tubular epithelium particularly in collecting tubules, pyelitis, cystitis. Climenko and Wright, *Arch. Path.*, 92: 791 (Nov.) 1911.

Man—

Blood Concentrations: 35 patients were given 1.0 gm. thrice daily to a total of 20 gm. in seven days. Blood concentrations were 9 mgm/100 ml. with good results, 20 mgm/100 ml. in renal diseases; 10 mgm/100 ml. should be greatest concentration for good clinical results. Ganem, *J.A.M.A.*, 117: 2198; 1911.

Neutropenia: 1,000 neutrophils per ml. after 0.5 gm. was given four times a day for 15 days. Malaise, headache, and pruritis of face resulted.

Neutropenia recurred on 29th day with 0.5 gm., also three months later with 0.12 gm. Desensitization carried out. Park, Lancet, 246: 401; 1914.

SULFARSPHENAMINE

Man—

Compared to Neoarsphenamine: Frequency of reactions for sulfarsphenamine and neoarsphenamine were respectively: icterus, 1.03/1000, 3.3/1000; purpura hemorrhagica, 2.85/1000, 0.44/1000; reactions in third course, 21.2/1000, 5.9/1000. Frequency of major reactions with sulfarsphenamine was 7.8 and rate of major reactions was 17.2/1000 white females. Probey et al., Pub. Health Rep., 59: 733 (June) 1944.

SULFASUXIDINE

Dogs—

Toxicity: Due to poor absorption, there was no oral toxicity. Intramuscularly, no toxic manifestations occurred, although considerable blood concentration was attained. 5 gm/kg. as monosodium salt given intravenously in 40% solution caused death. Poth et al., Arch. Surg., 44: 187 (Feb.) 1912.

Prevention of Purulent Peritonitis: After ligation of veins in a 50 cm. ileal segment of intestines in five of seven dogs through administration of 0.5 gm/kg. daily for ten days preoperatively. 18 controls and two of treated died within 48 hours. Sarnoff et al., Surgery, 16: 927 (Dec.) 1944.

SULFATHALIDINE

(Phthalyl sulfathiazole)

Dogs—

Toxicity: LD₅₀ was 2.5 gm/kg. per day orally. Intravenously, 10 ml. of 10% solution of sodium salt per kg. caused vomiting. Orally, 0.083 gm/kg. every four hours for six doses was not harmful, and blood concentration was not more than 3.3 mgm/100 ml. Poth and Ross, Texas Rep. Biol. Med., 1: 345; 1943.

SULFATHIAZOLE

Mice—

Acute Toxicity LD₅₀ of sodium salt was 1.32 ± 0.02 mgm/kg., intraperitoneally. Cranston et al., J. Pharmacol. & Exper. Therap., 81: 284 (July) 1944.

Cats, Rabbits, and Dogs—

Intracranial Implantation. 66 mgm., corresponding to 5 gm. in normal

man, when placed on cortex, led to convulsions in dogs and rabbits and in 50% of cats. At necropsy, animals killed weeks and months later, drug remained adherent to cortex. Pilcher, Angelucci, and Meacham, J.A.M.A., 119: 927; 1912.

Man—

Agranulocytosis: Resulted from 3 gm. daily for a total of 16 gm. plus aspirin compound. Thompson, Northwest Med., 41: 133 (Apr.) 1912.

Granulocytopenia: 7.5 gm. was taken in three days for throat infection. Death occurred 60 hours after admission in hospital. Critz, Arch. Pediat., 61: 154 (Mar.) 1914.

In Craniotomy: Two to 3 gm. used locally in six frontal craniotomy cases. Five resulted in epileptic seizures two hours after operation, two were fatal. Watt and Alexander, Lancet, 212: 493 (Apr.) 1912.

Death: 54 gm., given for gonorrhea, resulted in uremia, rash, hematuria, acute tubular nephritis, acute splenitis, and death. Gossler, South. M. J., 37: 365 (July) 1944. Patient became hypersensitive to 4 gm. given daily for five days and died on second course of 4, 5 and 6 gm. daily for three days, respectively. Fatal reactions were vascular and perivascular lesions, dermatitis, and anuria. Flynn, J. Iowa M. Soc., 35: 185 (May) 1915.

Salivary Levels: 67.1 mgm/100 ml. saliva was calculated average concentration of dissolved sulfathiazole for entire 60 minutes test period after one 0.25 gm. tablet was taken by 84 subjects, and average concentration was 78.4 mgm/100 ml. saliva with two tablets (0.5 gm.). Harrison and Rees, Am. J. Pharm., 117: 204 (June) 1915.

SULFATHIAZOLE SESQUIHYDRATE, SODIUM

Man—

Renal Function in Children: Intravenously, 0.1 gm. in 10 ml. sterile distilled water caused 14.5 to 37.1% to be excreted in two hours in children without kidney pathology, and only 7.5 to 20.1% to be excreted within two hours by children with kidney pathology. Kato, J. Pediat., 20: 576 (May) 1912.

SULFONAMIDES*

In Vitro—

Assay: Differentiation and identification of sulfanilamide, sulfapyridine, sulfathiazole, sulfaguanidine, and sulfadiazine. Calmari, Hubata, and Roth, Indust. & Engin. Chem., Anal. Ed., 11: 531 (July) 1912.

*Only critical pharmacologic and toxicologic data are included. For more detailed summary consult annotated bibliographies which are generally available.

Blood Sulfonamide Determination: Determination of blood sulfonamides from one drop of blood from finger tip. Peters, J.A.M.A., 124: 31; 1944.

Determination in Tablets: Bromination in 50 to 70% glacial acetic acid at room temperature was accomplished in two minutes. End point was sharp and stable, no external indicator was needed and excipient did not interfere. Conway, J. Am. Pharm. A. (Scient. Ed.), 34: 236 (Sept.) 1915.

Identification: Sulfanilamide, sulfathiazole, sulfadiazine, sulfapyridine, and sulfamerazine were identified as their crystalline cuprous complexes. 30 mgm. heated with 5 ml. Shaffer-Hartman reagent and 5 ml. 100 mgm.% glucose solution for five minutes on a water bath. Dodson and Todd, J. Lab. & Clin. Med., 30: 891 (Oct.) 1915.

Micromethod for blood sulfonamide determination. Jorgensen, J. Lab. & Clin. Med., 27: 1355 (July) 1912.

Use in Stored Blood: 0.19% sulfanilamide, 0.02% sulfadiazine, 0.05% sulfathiazole added to whole blood almost or completely prevented growth of three contaminating test strains of bacteria. Jensen, M. J. Australia, 30: 376 (Nov.) 1913.

Mice—

Excretion in Feces: 80 to 400 mgm/100 ml., sulfathiazole and 600 to 1300 mgm/100 ml., sulfaguanidine were excreted on diets containing 4% of drugs. Hawking, Lancet, 242: 290 (Mar.) 1912.

Rats (albino)—

Chronic Toxicity: 1% sulfonamides in diet caused depletion of mature granulocytes in bone marrow; necrosis and calcification of skeletal muscles; histocyte proliferation; calcification and hyalinization of one or more arteries in 10% of rats given sulfathiazole and in 3% given sulfanilamide, there were other pathologic changes. Endicott, Kornberg, and Daft, Pub. Health Rep., 59: 49 (Jan.) 1944.

Cats—

Concentration in Feces Orally, 0.5 gm/kg. produced 75 to 3800 mgm. of sulfaguanidine in 100 ml. of feces after 24 hours; 32 mgm. sulfanilamide in 100 ml. after 24 hours; 30 to 3400 mgm. sulfapyridine in 100 ml. in 48 hours; 1600 to 4900 mgm. sulfathiazole in 100 ml. in 24 hours; and 150 to 2800 mgm. sulfadiazine in 100 ml. in 24 hours. Hawking, Lancet, 242: 290 (Mar.) 1912.

Man—

Agranulocytosis: 10 gm. sulfanilamide initially, then 35 gm. sulfadiazine in four days, were followed two days later by 15 gm. sulfathiazole

in four days and finally 14 gm. sulfapyridine in two days. Death resulted despite treatment with 360,000 units penicillin, intramuscularly and 120,000 units, intravenously in three days. Cameron and Edge, Brit. M. J., I: 688 (Nov.) 1945.

Hemolytic Anemia: Three to 6 gm. of various sulfas given daily for six to 34 days produced some degree of hemolysis in the blood of 16 patients. Pachmilewitz, de Vries, and Hermon, Am. J. Clin. Path., 15: 381 (Sept.) 1945.

Blindness: Total of 38 gm. sulfathiazole in five days, given to a patient with bronchiectasis, previously given sulfapyridine for three weeks, caused complete atrophy of optic nerve. Monbrun and Laedrich, Am. J. Ophth., 28: 1100 (Oct.) 1945.

Hematuria: Developed in three patients given usual dosages of sulfapyridine, sulfathiazole, and sulfadiazine, blood concentrations of free drugs were: 3.2 mgm.%, 7.8 mgm.%, and 13.0 mgm.% respectively. Hematuria absent in others with blood levels of 30 to 50 mgm.%. Barnett, J. Missouri M. A., 41: 25 (Feb.) 1944.

Aerosol Inhalation: Microcrystals of average diameter of two to 4 micra caused no unfavorable reactions even in asthmatics; analgesia for two to three hours; purulent discharge disappeared temporarily. Chapple et al., Am. J. M. Sc., 207: 488 (Apr.) 1944.

Excretion in Feces: 384 to 2500 mgm. in 100 ml. feces within 24 hours after oral administration of 5 gm. sulfaguanidine. Hawking, Lancet, 242: 290 (Mar.) 1942.

Excretion in Normals: Orally, 3 to 5 gm. sulfanilamide and 3 to 6 gm. acetylsulfanilamide were given three and four hours respectively, prior to test and inulin, 1 gm. in 100 ml. saline by intravenous drip during and prior to test. Plasma concentrations during test were one to 15 mgm.% sulfanilamide, one to 5 mgm.% acetylsulfanilamide, and 10 to 60 mgm.% inulin respectively. Mean clearance of sulfanilamide was 0.15 times as great as that of inulin and acetylsulfanilamide was almost identical with inulin. Loomis, Koepf, and Hubbard, Am. J. Physiol., 141: 158 (Mar.) 1944.

SULFUR-POLYSULFIDE

Man—

Rheumatic Fever in Children: Orally, 250 mgm. of colloidal sulfur polysulfide, daily produced more nearly complete recovery in treatment of 15 than in controls. Greengard, Elghammer, and Ivy, Am. J. Dis. Child, 63: 659 (Apr.) 1942.

SUPRARENAL CORTEX EXTRACT (Eucortone)

Man—

Cholera: Intravenously, 2 ml. in 100 ml., 25% glucose followed by saline infusions gave good results. Lahiri, J. Indian M. A., 14: 113 (Mar.) 1915; through Trop. Dis. Bull., 42: 613 (Aug.) 1915.

SYNEPHRINE TARTRATE

(d,1-hydroxy-methylamino-4-hydroxyethyl-benzene hydrochloride)

Man—

Effect: Threshold effect: subcutaneously, 90 to 115 mgm. produced five to 10 mm. Hg rise in systolic blood pressure, no change in diastolic pressure or heart rate in ten to 30 minutes. Therapeutic dose for pressor action was 400 mgm. given subcutaneously. Intravenously, 20 mgm. produced a sharp rise in systolic blood pressure and fall in pulse rate. Keys and Violante, J. Clin. Investigation, 21: 13 (Jan.) 1912.

TANNIC ACID

Rats—

Liver Damage was in direct proportion to amount injected. No more than 1.5 ml. of 5 to 10% solution was given subcutaneously at any one site. Wells et al., New England J. Med., 226: 629 (Apr.) 1912.

Sodium tannate, pH 7.2 was as toxic as pH 3 solution, subcutaneously. Applied by 15 minute bath to denuded area (ventral skin removed) and washing next day, even 2.5% solution produced liver necrosis with one-fourth of body area involved. 20% solution caused severe necrosis and death. Hartman and Romence, Ann. Surg., 118: 402 (Sept.) 1943.

Dogs—

Liver Damage: Sodium tannate, pH 9, 10 to 20 ml. of 7% solution daily, subcutaneously, produced no reaction, but consistently liver necrosis with jaundice and death. Hartman and Romence, Ann. Surg., 118: 402 (Sept.) 1943.

Man—

Burn Therapy: Patient anesthetized, burned area cleansed with soap and brush, benzine and alcohol. Dried with warm air, sprayed with 5% tannin, dried and sprayed with 10% silver nitrate. Tetanus antitoxin given. Tannin preferable for face burns and had analgesic effect. Used advantageously only for first to third degree burns, not on fourth and fifth degree burns. Gey, Deutsche Militärarzt, 6: 287 (May) 1942; through J.A.M.A., 119: 982; 1942.

Liver Damage: 93% under tannic acid therapy showed hepatic damage. Hepatotoxic and retarded epithelization in burn therapy. Lee et al., Pennsylvania M. J., 48: 563 (Mar.) 1945.

Liver Dysfunction resulted in five of eight children in treating burns with jelly containing 5% tannic acid and 1:5000 merthiolate. Rae and Wilkinson, Lancet, 246: 332; 1944.

TESTOSTERONE

Rats—

Spermatogenesis: Very small doses (possible absorption was 12.5 micrograms per day) administered intratesticularly to hypophysectomized rats for 70 to 120 days, maintained spermatogenesis. Same effect was obtained with one to 3 mgm. per day extratesticular administration. Dvoskin, Proc. Soc. Exper. Biol. & Med., 54: 111 (Oct.) 1943.

Dogs—

Alopecia: Twelve intramuscular injections of 5 mgm. at two and three day intervals produced hair in two months in pomeranians. Edgett, North American Veterinarian, 24: 675 (Nov.) 1943.

Geldings—

Muscular Endurance increased with subcutaneous implantation of 150 to 525 mgm Kearns, J. Am. Vet. M. A., 100: 197, 1942.

Man—

Muscular Endurance: 100 mgm., orally, daily for 21 days was given to castrates. Ibid.

TESTOSTERONE, ETHINYL

Mice (male)—

Mammary Glands: One to 2 mgm per week in two injections (subcutaneously and intraperitoneally, respectively) for three to six weeks caused morphological development of mammary plexus without producing glandular secretion, glands resembled those of adult virginal or non-pregnant females. Chamorro, Compt. rend. Soc. de biol., 138: 71 (Feb.) 1944.

TESTOSTERONE, 17-METHYL

Man—

Eunuchoidism Therapy 25 mgm daily was given to a boy, and 25 mgm. three times a day orally, to three adult males Byron and Katzen, J. Clin. Endocrinol., 1: 359 (Apr.) 1941.

Menopause Therapy: Five to 25 mgm., orally, daily for one to six

months for a total of 750 to 3565 mgm. was given. Kurzrok and Rothbast, *Am. J. Surg.*, 56: 636 (June) 1912.

Work Capacity was increased with 40 mgm. oral daily doses for three to six weeks; duration up to eight months. Simonson et al., *J. Clin. Endocrinol.*, 4: 528 (Nov.) 1914.

TESTOSTERONE, METHYL

Man—

Excretion: 20 to 200 mgm. daily decreased average urinary excretion of 17 ketosteroids from 18.7 mgm. to 11.9 mgm. Reifenstein et al., *J. Clin. Investigation*, 24: 416 (July) 1915.

Menopause Therapy: Orally, 20 mgm. daily for four weeks followed by 10 mgm. for two weeks with several intermittent one week intervals during which drug was withdrawn was the most effective dosage schedule. Gusberg, *Am. J. Obst. & Gynec.*, 50: 502 (Nov.) 1915.

Sublingually, 5 to 30 mgm. in tablet form daily for several weeks. Joel, *J. Clin. Endocrinol.*, 2: 116 (Feb.) 1912.

Myasthenia Gravis: Orally, 50 mgm. daily for two weeks, then by 30 mgm. per day for four weeks and 20 mgm. per day for two weeks. One patient improved in 48 hours after taking 75 mgm. prostigmine bromide daily, simultaneously. *Queries & Minor Notes, J.A.M.A.*, 121: 70; 1944.

Simmonds' Disease: Sublingually, 20 mgm. daily for ten days, 15 mgm. daily for six weeks, 5 mgm. daily for three months, and then 10 mgm. daily thereafter restored sexual deficiencies in a patient previously refractory to various pituitary preparations. Lisser and Curtis, *J. Clin. Endocrinol.*, 5: 363 (Nov.) 1915.

Sublingual Administration: Dose determined by trial, but 10 to 20 mgm. was considered as probable required amount. Spence, *Brit. M. J.*, I: 668 (May) 1942.

TESTOSTERONE PROPIONATE

Rana Clamitans Larvae—

Sex Reversal: Injections weekly of 0.25 mgm. per week for a total of 4 mgm. in 95 days, 0.05 mgm. per week for a total of 0.9 mgm. in 123 days; and 0.025 mgm. per week for a total of 0.525 mgm. in 141 days obtained complete sex reversal from females to males. Mintz, Foote, and Witschi, *Endocrinology*, 37: 286 (Oct.) 1915.

Fowls—

Tissue Strength. A total of 50 mgm. given through a period of 20 days

to young female and capon fowls showed that skin had nearly 100% greater tensile strength than that from untreated birds. Herrick, *Anat. Rec.*, 93: 145 (Oct.) 1945.

Chickens (Single Comb White Leghorn females)—

Genital Tract: Intramuscularly, 6 mgm. caused growth of genital tract. Herrick, *Poultry Sci.*, 23: 65 (Jan.) 1944.

Opossum Embryos—

Bisexual Differentiation. Minimal effective dose was 10 to 15 gammas per day at which the Mullerian duct ceased to react. Burns, *J. Exper. Zool.*, 100: 119 (Oct.) 1945.

Rats—

Biochemical Effects in castrated rats. Subcutaneously, 0.1 mgm. and 0.2 mgm. daily, to male and female castrated rats, respectively, showed no change in serum calcium or phosphorus, nor their output in the feces. Buchwald and Hudson, *Endocrinology*, 37: 301 (Nov.) 1945.

Comparison of Administrations. Intraperitoneal injections for ten days showed 274% increase in seminal vesicular growth, 41.9% decrease in testicular size, and 11% decrease in body weight. Subcutaneous injections caused 185% increase in seminal vesicular growth, 52.8% decrease in testicular size and no difference in weight gain. Rubinstein, *Proc. Soc. Exper. Biol. & Med.*, 51: 230 (Nov.) 1942.

Effect of Large Doses in castrate albino rats. 1 mgm. daily for 26 to 80 days depressed body weight and length. Rubinstein and Solomon, *Endocrinology*, 28: 112; 1941.

Corpora Lutea: Subcutaneously, 2.5 to 5.0 mgm. given for ten days caused deciduata formation in traumatized uterus. 5 mgm. plus 400 international units of prolactin produced large corpora lutea, although each alone was ineffective. Fluhmann and Laqueur, *Proc. Soc. Exper. Biol. & Med.*, 54: 223 (Nov.) 1943.

Thymic Atrophy: Intramuscularly, 6.6 to 13.5 mgm. in oil prevented regeneration of thymus cortex previously destroyed by exposure to X-rays. Subcutaneous implantation of 1.2 to 2.2 mgm. estrone produced similar effects. Grégoire, *Arch. internat. de pharmacodyn. et de therap.*, 70: 45 (Jan.) 1945.

Rats (albino, males)—

Chronic Toxicity: Groups received intraperitoneally, daily 1 mgm., 100 gammas, and 50 gammas, respectively. Body weight showed trend toward depression; testes were inhibited in growth, seminal vesicles and epididymus were stimulated. Rubinstein, *J. Urol.*, 51: 88 (Jan.) 1944.

Guinea Pigs—

Effect: Subcutaneously, 4 mgm. on alternate days for 20 days in adult spayed animals and 2 mgm. on alternate days for 30 days to immature animals produced hypertrophy of clitoris, vaginal changes, uterine enlargement, and follicular stimulation. Bacsich, Sharman, and Wyburn, J. Obst. & Gynaec. Brit. Emp., 52: 334 (Aug.) 1945.

Monkeys—

Experimental Menstruation postponed by 1 mgm. after 50 gammas of estrogen were given daily for ten days. Duncan, Allen, and Hamilton, Endocrinology, 28: 107; 1941.

Monkeys, Rhesus—

Conversion to Androsterone: 1.2 gm. administered to three pregnant monkeys and urine collected for 70 days. 22 mgm. of androsterone was isolated, which was not present in urine of monkeys not receiving testosterone. Horwitt, Dorfman, and van Wagenen, Endocrinology, 34: 351 (May) 1944.

Man—

Angina Pectoris Therapy: Intramuscularly, 25 mgm. twice weekly for eight weeks produced improvement in seven of ten patients. Waldman, J. Clin. Endocrinol., 5: 305 (Sept.) 1945.

Twelve injections of 25 mgm. at four to five day intervals brought improvement. Strong and Wallace, Canad. M. A. J., 50: 30 (Jan.) 1944.

Arteriosclerosis Obliterans Therapy: No benefit was observed with intramuscular injections of 25 mgm. biweekly for three to 18 months in 8 patients. Zurrow et al., J. Lab. & Clin. Med., 28: 268 (Dec.) 1942.

Aspermin Therapy: Intramuscularly, 10 to 50 mgm. two to three times a week for six weeks, then twenty-one 25 mgm. injections during two months, and six 50 mgm. injections for one month. Huhner, J. Urol., 51: 178 (Feb.) 1944.

Breast Cancer: 25 mgm. on alternate days for a total of 250 mgm. caused subsidence of pain and vomiting. With 700 mgm. fibroma disappeared. Reactions were intense pain in lower abdomen, sensation of impending menstruation, virilization with a total of 1,550 mgm. Fels, J. Clin. Endocrinol., 4: 121 (Mar.) 1944.

Pelvic Cancer: 10 mgm. three times weekly, increased to 20 mgm., and later 30 mgm. three times weekly in two patients; and 25 mgm. three times weekly were given to four patients. Rapid relief from pain without size reduction or change in neoplasm were observed. Beecham, Am. J. Obst. & Gynec., 46: 849 (Dec.) 1943.

Functional Prepuberal Castration was treated with 25 mgm. injections five times weekly for three to four months in six men of 19 to 57 years. Heller, Nelson, and Roth, *J. Clin. Endocrinol.*, 3: 573 (Nov.) 1943.

Diabetes Mellitus and Addison's Disease Intramuscularly, 25 mgm. in oil daily for three days and 25 mgm. in oil daily for three days and 25 mgm. in oil daily for three days.

Vigor :

Endometrial Tumor: Intramuscularly, 25 mgm. in oil, twice weekly for 12 weeks reduced tumor, ameliorated diarrhea and pain during menstruation, facilitated operative removal. Miller, *J. A. M. A.*, 125: 207; 1944.

Eunuchs: 50 mgm. three times a week relieved physically and psychologically. Frank, *Am. J. Obst. & Gynec.*, 47: 561 (Apr.) 1944.

Genitalia Malignancy in women. Treated with 140 to 150 mgm. weekly for ten months in five patients. There was symptomatic improvement, no regression or retardation of malignant process. Abel, *Am. J. Obst. & Gynec.*, 49: 327 (Mar.) 1945.

Gerontotherapy: Injection of 5 to 10 mgm. twice weekly in ageing man and 5 mgm. for ten weeks, repeated twice yearly for a man over 70 acted as a tonic. Benjamin, *Urol. & Cutan. Rev.*, 48: 17 (Jan.) 1944.

Pruritis Vulvae (menopausal): Treated with vitamin A and preparation containing 2 mgm. propionate to 1 gm. of ointment. Cinberg, *Am. J. Obst. & Gynec.*, 49: 647 (May) 1945.

Vigor Increased: Muscle atrophy and weakness in 88 year old man was controlled by implantation of eight pellets of 100 mgm. and maintained for ten months. Binet and Verhae, *Compt. rend.*, 216: 430 (Mar.) 1943.

Nitrogen Excretion: Intramuscularly, 25 mgm. daily for eight days preceding and for six days of fasting period reduced total nitrogen, urinary nitrogen, and creatine nitrogen, 33, 34, and 1.6 mgm./kg. per day, respectively. Butler et al., *J. Clin. Endocrinol.*, 5: 327 (Oct.) 1945.

Gastric Secretion: Intramuscularly, 2 to 100 mgm. daily for four days or intravenously, 4 ml. whole testicular extract daily for four days increased levels of free and total hydrochloric acid and increased total gastric secretion. Intramuscularly, 100 mgm. for ten days increased gastric acidity in achlorhydria. De Muro and Marconi, *Rev. Gastroenterol.*, 12: 363 (Sept.-Oct.) 1945.

TETANUS ANTITOXIN

Dogs—

Experimental Tetanus 100 dog lethal doses of toxin required 182 to 200 times the neutralizing dose of antitoxin in six hours, and 300 times

in seven hours to save dogs. Thompson and Friedman, Surg., Gynec. & Obst., 72: 860; 1941.

Tetanus in Great Dane: Recovered from intraspinal administration of 9000 units twice, intravenously, 50 ml. 50% glucose, subcutaneously, 1 liter saline plus glucose; intravenously, 25 ml. 25% magnesium sulfate and same amount, intraperitoneally. Gockjian, Vet. Med., 37: 141 (May) 1942.

Man—

Immunization Reaction: 1500 units administered to a veteran previously given toxoid produced a severe incapacitating reaction. Freedman, J.A.M.A., 129: 1045; 1945.

Tetanus Therapy: Intravenously or intramuscularly, 20,000 to 100,000 units, also tribromethanol and sodium amytal. Spaeth, Arch. Int. Med., 68: 1133 (Dec.) 1941.

60,000 units for severe cases, and 40,000 units for mild cases. Spaeth, Am. J. Dis. Child., 61: 1146; 1941.

Intravenously, initial dose of anti-tetanic serum of 50,000 units, thereafter 5000 units daily. At initial injection time 10,000 units were infiltrated into surrounding tissues in preparation of wide incision of wound. Intrathecally, 15,000 to 20,000 units by lumbar puncture or intracisternally. Firor, Internat. Abstr. Surg., 75: 185 (Aug.) 1942. Intravenously or intramuscularly, 200,000 international units, repeated in 50,000 international units weekly doses in weekly intervals in severe wounds, by excision of wounds and control of reflex spasm with paraldehyde or tribromethanol. Cole, Brit. M. J., II: 550 (Nov.) 1942.

If tetanus antiserum was simultaneously injected intravenously and intrathecally, further development of disease was averted and patient recovered. Suboccipital injection of 10 to 20 ml. antiserum could be repeated in same patient if corresponding amount of spinal fluid was removed. Stern, Illinois M. J., 84: 387 (Dec.) 1943.

Immediate use of antitoxin, 70 to 90 mgm/kg. tribromethanol every six hours for restlessness, 0.13 gm. phenobarbital every four hours, and sodium amytal intravenously to control convulsions. Vinnard, Surgery, 18: 482 (Oct.) 1945.

Intramuscularly, 40,000 to 50,000 units of antiserum daily were given to those whose original foci of infection could not be found or completely removed. 45% mortality in 352 patients. Methods to reduce mortality were given. Ibid.

Intravenously or intramuscularly, 25,000 units of antitoxin was the

optimum dosage. Administration was ineffective in majority of patients. Gessler, J. Tennessee M. A., 38: 363 (Nov.) 1945.

TETANUS TOXIN

Rabbits—

Blood: 0.3 minimal lethal dose, intravenously or intramuscularly caused 50 to 60% decrease in red blood cells, decrease in hemoglobin, and increase in sedimentation rate. Recovery with antitoxin. Farkas and Kligler, Proc. Soc. Exper. Biol. & Med., 48: 717 (Dec.) 1941.

TETANUS TOXOID

Mice—

Assay (mouse protection test). Tolerance of at least 24 toxoid-immunized white mice for 15 minimal lethal doses of tetanus toxin were tested. Lahiri, Indian J. M. Research, 30: 371 (July) 1942.

Mice (Swiss)—

Standardization and Assay: Mice were standardized (at least 20 each of male and female) for their antigenic response by repeated tests using provisional standard toxoid. Injected animals rested for 21 days and then were subcutaneously injected with ten minimal lethal doses of aged tetanus toxin of constant titre. They were observed for seven days and average number of protected animals recorded. This figure represented standard value of protection for chosen strain of Swiss mice. Two groups of mice received injections of tetanus toxoid under trial and of standard toxoid, respectively. After two weeks, ten minimal lethal doses of aged tetanus toxin of constant titre were injected. Protection from unknown toxoid was then compared with that of standard toxoid tested simultaneously. Koerber and Mook, Proc. Soc. Exper. Biol. & Med., 51: 299 (Nov.) 1942.

Man—

Prophylaxis: Subcutaneously, 1 ml. toxoid, followed in one to three months by a similar injection. Firor, Internat. Abstr. Surg., 75: 185 (Aug) 1942.

TETRACAINE HYDROCHLORIDE

Mice (white)—

Toxicity: Minimal lethal dose was 70 mgm/kg., intraperitoneally. Co Tui, Anesth. & Analg., 22: 301; 1943.

Guinea Pigs—

Toxicity: Intramuscularly, 30, 25, 20, 15, and 10 mgm. per kg. killed 100, 80, 33.3, 4.1, and 0% of animals, respectively. Toxicity reduced by

injection of sodium, potassium and calcium gluconates, levulinates, and lactates 18 to 20 minutes before injection. *Wastl, Anesth. & Analg.*, 21: 218 (July-Aug.) 1942.

Man—

Atelectasis Therapy: Spraying 2% solution or 10% cocaine to anesthetize posterior pharynx and epiglottis. Mucus was withdrawn by suction through a urethral catheter passed into trachea. *Thompson, U. S. Nav. M. Bull.*, 44: 757 (Apr.) 1945.

Bronchiectasis: 2% solution (3 ml.) and a 1:1000 solution of epinephrine (1.0 ml.) was mixture sprayed on lips, mouth and throat and larynx, and instilled into trachea to obtain satisfactory bronchogram. This amount was reduced for children. *Harwood, M. J. Australia*, 1: 65 (July) 1945.

Bronchoscopies: Local anesthesia with 2% solution was used for poor risk patients or those with severe heart conditions. *Valle, Surg., Gynec. & Obst.*, 81: 278 (Sept.) 1945.

Fatality: Intranasal administration of 2 ml. of 2% solution caused fatal convulsions. *Doane and Cohn, Anesthesiology*, 6: 421 (July) 1945.

Caudal Anesthesia: 20 to 30 ml. of 0.25% was effective for 45 to 60 minutes; 20 to 30 ml. of 0.1% with 1:200,000 epinephrine was effective for 60 to 120 minutes. Severe nausea and vomiting in two; postpartum atony of bladder in three. *McClellan and Williams, Am. J. Obst. & Gynec.*, 48: 617 (Nov.) 1944.

Fractional Spinal Anesthesia: 0.4% solution plus 3.3% procaine hydrochloride in 6% glucose used in operation in which contemplated duration was unpredictable or would exceed time usually permitted by spinal anesthesia. *Hand, Anesth. & Analg.*, 21: 189 (July-Aug.) 1942.

Spinal Anesthesia: 15 mgm. was used for perineal or leg work, and 20 mgm. for abdominal work including operation of diaphragm. Duration lasted two to three hours. There were no marked blood pressure changes, postoperative complications, and morbidity was minimal. *Ramond, Illinois M. J.*, 82: 141 (Aug.) 1942.

TETRACHLORETHANE

Man—

Fatality: Jaundice, pain in right upper abdominal quadrant, and tenderness on palpitation. Red blood cells fell from 4,470,000 to 4,090,000 in three days. Fatigue, loss of appetite, nausea and vomiting. Bile in urine, clay stools. *Autopsy findings were:* "cirrhosis of liver with superimposed hepatitis; severe jaundice; hypertrophy of heart; hemorrhagic

diathesis with bleeding into gastrointestinal tract, and ascites." Coyer, *Indust. Med.*, 13: 230 (Mar.) 1944.

Symptoms of Poisoning. Nausea, heartburn, palpitation, vomiting, gastric pain, anorexia, headache and dizziness. Jaundice appeared on long exposure and tremor and nerve paralysis appeared temporarily. Nephritis, various degrees of anemia and heart murmurs were observed. 25 of 1000 showed rise of icterus index Wilson and Brumley, *Indust. Med.*, 13: 233 (Mar.) 1944.

Treatment of Poisoning: Intravenously, 1 liter of 5% glucose once or twice daily, forced fluids, bland diet, liver and iron for anemia and transfusion for severe cases. *Ibid.*

13 of 14 slowly recovered with bed rest, intramuscular injection of 1 ml. liver extract daily, 25 ml. of 50% or 1 liter of 5% glucose injected daily with saline; and a high carbohydrate diet Coyer, *Indust. Med.*, 13: 230 (Mar.) 1944.

TETRACHLORETHYLENE

Man—

Teniasis. Maximum dose of 4 ml. cleared 30 after one treatment. Cure rate was 54%. Mukerji and Maplestone, *Indian M. Gaz.*, 78: 282 (June) 1943; through *Trop. Dis. Bull.*, 40: 925 (Dec.) 1943.

TETRACHLORODIPHENYLETHANE

(T D E)

Mosquitoes—

Anopheline Larvicide. 0.01 part per million in acetone suspension was effective in 1.166 hours, and a similar suspension of DDT in 0.81 hour. TDE dust was superior to DDT against *Anopheles quadrimaculatus*. 0.5% TDE in fuel oil solution caused 100% mortality in 48 hours, and 76.6% mortality with 0.5% DDT. Deonier and Jones, *Science*, 103: 13: 1946.

TETRAETHYL AMMONIUM BROMIDE

Dogs—

Heart-lung Preparation. 1:100,000 (48 micromols per liter) improved working capacity of heart, produced changes in "T"-wave and S-T segment of electrocardiogram. 200 mgm. produced cardiac irregularities with pentobarbital. Acheson and Moe, *J. Pharmacol. & Exper. Therap.*, 84: 189 (June) 1945.

Dogs and Cats—

Effect: 25 mgm. or more per kg. produced same effects in anesthetized animals as in heart-lung preparation. *Ibid.*

TETRAHYDRO β -NAPHTHYLAMINE**Cats—**

Bulbocapnine Antagonism: Catalepsy produced by 25 mgm/kg. bulbocapnine subcutaneously, lasting normally for four to five hours, was completely abolished by 10, 5 or 2.5 mgm/kg. within 20 to 30 minutes. Administration simultaneously with bulbocapnine prevented catalepsy and produced no symptoms. Kerman, Arch. Neurol. & Psychiat., 52: 61 (July) 1944.

THEOBROMINE CALCIUM GLUCONATE**Man—**

Hypotensive Action: Orally, one to two tablets (each tablet containing 0.3 gm. and 0.15 gm. theobromine and calcium gluconate respectively) three times daily to 30 patients with blood pressures ranging from 158/100 to 250/100, for a few weeks to six months (mean was two months). 20 mm. Hg or more reduced in 80%, others averaged 11 mm. Hg. There were no untoward reactions. Wipperfurth and Gunn, M. Times, New York, 70: 197 (June) 1942.

THEOBROMINE, 1-ETHYL**Man—**

Oral Toxicity: 20 mgm. each taken by six adults for three separate days caused no untoward effect. Scott and Chen, J. Pharmacol. & Exper. Therap., 82: 89 (Sept.) 1944.

THEOBROMINE SODIUM ACETATE**Dogs—**

Experimental Coronary Occlusion: Animals saturated with 450 mgm. orally for several days before occlusion and received intramuscularly 120 mgm. immediately after, did not die. Le Roy, Fenn, and Gilbert, Am. Heart J., 23: 637 (May) 1942.

THEOPHYLLINE COMPOUNDS**Mice—**

Toxicity: Minimal lethal dose in mgm/gm. body weight was subcutaneously, 0.2 mgm. for theophylline sodium acetate; 0.14 mgm. for theophylline plus ethylenediamine (aminophylline); 0.16 mgm. for theophylline plus ethylenediamine plus phenobarbital (novophylline); and 0.15 mgm. for theophylline plus diethanolamine (deriphyllin). Lethal dose of theophylline was reduced 20 to 25% by addition of ethylenediamine and diethanolamine. Oelkers, Arch. f. exper. Path. u. Pharmacol., 197. 193; 1941.

THEOPHYLLINE AMINOISOBUTANOL**Man—**

Angina Pectoris 0.18 gm three times a day for periods of four weeks failed to reduce incidence of attacks in ten patients. Steinberg and Jensen, J Lab. & Clin Med., 30 769 (Sept) 1915.

THEOPHYLLINE ETHYLENEDIAMINE

(Aminophylline)

Guinea Pigs—

Antispasmodic Action Epinephrine was 1000 times more effective on isolated lungs than aminophylline or theocine in relieving constriction caused by histamine, pilocarpine or barium Ludueña, J Pharmacol. & Exper. Therap., 75: 316 (Aug) 1912

Rabbits—

Chronic Toxicity: Intravenously, 7 mgm/kg daily for one month showed no toxicity. Highest single tolerated dose was 100 mgm/kg., intravenously. Ibid.

Dogs—

Antispasmodic Action. Epinephrine was 3000 times more efficient on bronchi in situ than aminophylline or theocine, but dilating action of latter two were more sustained Ibid

Man—

Best Diuretic: 0.5 gm., and one hour later 1 ml. of mersalyl solution was given intramuscularly. Result was unequaled by any other combination, except by 4 ml. mersalyl given alone Goodman, Corsaro, and Stacy, Arch. Int. Med., 70. 975 (Dec.) 1912.

THIAMINE HYDROCHLORIDE**Frogs—**

Effect on Heart: 100 mgm. per 100 ml of Harvard Ringer's solution increased tonus of exposed heart. Larger concentration was a general cardiac depressant due to acidity and hypertonicity 100 and 250 mgm. per 100 ml. prevented bradycardia from chlorobutanol, strophanthin, arecoline, physostigmine and acetylcholine. Boyd and Dengwall, Quart. J. Pharm. & Pharmacol., 14 209 (July Sept) 1911.

Chickens—

Egg Content: 5 micrograms per gm. of diet fed to white leghorns, Rhode Island reds and barred rocks produced eggs with an average of 279, 167, and 175 micrograms per gm of yolk, respectively, and 105, 61,

and 66 micrograms per 100 gm. of egg content, respectively. Scrimshaw, Hutt, and Scrimshaw, *J. Nutrition*, 30: 375 (Nov.) 1945.

Mice (albino)—

Massive Dose Effect: 625 to 750 micrograms average daily intake during growth and 2,000 micrograms per day were given during lactation; manganese chloride 3 mgm. per day during growth and 8 mgm. per day during lactation were given for three generations. Did not affect reproduction, lactation, or growth rate. Cerecedo and Vinson, *Proc. Soc. Exper. Biol. & Med.*, 55: 139 (Feb.) 1944.

Rats—

Absorption in hyperthyroid and normal females: Absorption after 100 mgm./100 gm. weight was rapid during first hour and about equal in both. Stockholm, Althausen, and Bosson, *Proc. Soc. Exper. Biol. & Med.*, 46: 387; 1941.

Deficiency: 4 micrograms given daily for six weeks, withdrawn until definite signs of deficiency appeared, then subcutaneously, 50 micrograms were given, again no thiamine was given until acute symptoms reappeared. 57 died after 33 to 145 days (average 63 days). Enlarged heart due to dilatation of right auricle, nine had one to 2 ml. fluid in thoracic cavity, and microscopic pathologic changes were observed. Ashburn and Lowry, *Arch. Path.*, 37: 27 (Jan.) 1944. Intraperitoneally, 250 micrograms per day exerted a greater effect on work-performance in deficient animals than those on adequate thiamine diet. Kniazuk and Molitor, *J. Pharmacol. & Exper. Therap.*, 80: 362 (Apr.) 1944.

Galactose Absorption: 66% more galactose was absorbed by rats fed on diet supplemented with 40 micrograms thiamine daily. Leonard and Free, *J. Nutrition*, 26: 499 (Nov.) 1943.

Requirement: 33 micrograms daily was required for ten adult albino rats on diet of 64% sucrose, 20% casein, and 10% hydrogenated cottonseed oil, and 20 micrograms on 64% casein, 19.6% sucrose and 10% hydrogenated cottonseed oil diet. Wainio, *J. Nutrition*, 24: 317 (Oct.) 1942.

Cats—

Deficiency and Cure: Two cats on vitamin B₁ deficient diet for three weeks lost 20% of body weight, showed muscular weakness, disturbances of postural tone, walking and righting reactions, lessening of pupillary constriction in bright light, anorexia and clonic and spastic convulsions. One hour after injection of 1 mgm. (333 units), muscular coördination returned, convulsions no longer evoked; recovery practically complete. Everett and Saith, *Anat. Rec.*, 84: 481 (Dec.) 1942.

Thiamine Depletion was treated with subarachnoid injections of 0.5 to 2.0 mgm. in aqueous solution or normal saline. Odom and McEachern, *Proc. Soc. Exper. Biol. & Med.*, 50: 28 (May) 1942.

Dogs—

Blood Regeneration More than 10 micrograms per day caused no disturbance of hematopoietic function. Maass et al., *Arch. Biochem.*, 4: 105 (Apr.) 1944.

Foxes—

Chastek Paralysis was treated with intravenous injections of 3,000 to 9,000 units on two succeeding days to animals showing loss of appetite and neurologic symptoms, and 6,000 to 18,000 units daily injections for paralysis. Green et al., *J. Am. Vet. M. A.*, 100: 394 (May) 1942. Developed with 2 mgm. and diet containing 20% whole carp, 5 mgm. developed transient anorexia, 10 mgm. daily did not. Paralysis did not develop when fish and vitamin B₁ were given on separate days. Green, Carlson, and Evans, *Am. Fur Breeder*, 3: 16, 1943, through *Exper. Sta. Rec.*, 90: 251 (Feb.) 1944.

Horses—

Azoturia: Subcutaneously, 10,000 to 15,000 units per 45 kg. administered every 12 to 24 hours as needed brought recovery in six hours to seven days. Patton, *Vet. Med.*, 39: 10 (Jan.) 1944.

Man—

Deficiency: In children, average thiamine content in skeletal muscles was from 0.21 to 1.47 mgm/gm. and 0.14 to 0.21% phosphorus. Highest content for youngest. Less than 0.6 mgm/gm. of muscle, appeared to be abnormal for very young children. Hulse et al., *Am. J. Dis. Child.*, 67: 30 (Jan.) 1944.

Deficiency Test: Excretion of less than 50 gammas in urine within four hours after injection of 1 mgm. indicated deficiency. Holt, *Federation Proc.*, 3: 171 (Sept.) 1944.

Avitaminosis was treated with subcutaneous injection of 60 mgm. per day and intramuscularly, 2 ml. liver extract three times a week for 50 days plus high caloric, high vitamin diet, which produced rapid response in a patient with spinal cord damage resulting from vitamin deficient diet. Shulack and Peters, *J. Nerv. & Ment. Dis.*, 102: 359 (Oct.) 1915.

Polyneuritis caused by absorption of carbon tetrachloride through hands, was cleared by 100 mgm. B complex subcutaneously, and 10 mgm. thiamine, orally three times a day for 52 days. Farrell and Senseman, *Rhode Island M. J.*, 27: 334 (July) 1944.

Beriberi Heart in Infant: 6 mgm. daily added to diet. X-rays four years later showed cardiac shadow within normal limits. Rascodd, J.A.M.A., 120: 1292; 1912.

Beriberi Therapy: 5 to 100 mgm. daily, an average of 10 to 30 mgm. was given orally, subcutaneously, intravenously, intramuscularly or intraspinally, supplementary to highly nutritious and well balanced diet. Austria, Clinics, 2: 882 (Dec.) 1913.

Metabolism: Orally, 15 mgm. given to three normals was followed within six minutes by distinct rise in thiamine and greater and lasting rise of diphosphothiamine blood levels. Intravenously, 15 mgm. caused higher thiamine rise and less of diphosphothiamine in patients with liver cirrhosis. Thiamine excretion in one hour was 0.6% of oral and 2.8% of intravenous dose in normals, and patients with cirrhosis of liver and nephritis 4.7 and 1.4% of intravenous dose. Williams, Bissell, and Peters, Arch. Int. Med., 73: 203 (Mar.) 1914.

Excretion: Sweat concentration was 71 times that of urine in men fortified with 50 mgm. of thiamine and 750 mgm. ascorbic acid before taking one hour exercise, and 8.5 times urine concentration of thiamine after additional half an hour of exercise. Hardt and Still, Proc. Soc. Exper. Biol. & Med., 48: 701 (Dec.) 1911. 27.2% or 268 micrograms were excreted in urine with 990 microgram intake. Less than 20% excreted by the ill. With adequate diet containing 45 micrograms per 100 calories, excretion of less than 20% required supplementing of diet to secure tissue saturation. Benson et al., J. Pediat., 20: 454 (Apr.) 1912.

Excretion in Pregnancy: 3.39 international units was average amount excreted in urine in 24 hours by 46 normal pregnant. 24 hour urinary output in international units were: 3.58 for 28 hypertensive, 2.23 for six hyperemesis, 2.66 for 14 edema, 2.86 for three pre-eclampsia, and 0.94 for nine eclampsia cases. Nixon, Wright, and Fieller, Brit. M. J., 1: 605 (May) 1942.

Human Milk Content: 9.5 gammas per 100 ml. in third week of lactation to maximum of 14.8 gammas per 100 ml. in about 20th week. Slater and Rial, M. J. Australia, 1: 3 (Jan.) 1942.

Tissue Concentrations. There were 2 to 3 micrograms/gm. heart muscle, 0.5 microgram/gm skeletal muscle and 1 microgram/gm. liver, kidney, and brain tissue. Total for average person was 25 mgm. Ferrebee et al., J. Clin. Investigation, 21: 401 (July) 1912.

Adult Requirement: 350 micrograms per 1000 calories. Recommended daily intake was 500 micrograms per 1000 calories. Below critical level

of 0.7 to 1.0 mgm. per day, percent excretion of dietary thiamine decreased markedly. Melnick, J. Nutrition, 21: 139 (Aug.) 1942.

Requirement in Women: Minimal was 0.22 to 0.50 mgm. for each 1000 calories of diet. Optimal was not less than 0.5 mgm. and not more than 1 mgm. for each 1000 calories of diet. Williams et al., Arch. Int. Med., 69: 721 (May) 1942.

651 micrograms and thiamine vs. caloric ratio about 0.35 was requirement for women. Elsom et al., Am. J. M. Sc., 203: 569; 1912.

Requirement in Infant (breast fed): Marginal requirement was 0.36 gammas for each non-fat caloric, optimal was equal to or less than 0.62 gammas for each non-fat caloric. Slater and Rial, M. J. Australia, 1: 3 (Jan.) 1942.

Cardiacs: Administration of vitamin B recommended to cardiacs with dietary restrictions to eliminate development of beriberi. Parenteral administration of eight 30 mgm. doses cleared beriberi in patient under dietary regime to control arteriosclerosis heart disease. Warshawsky and Weissberg, M. Bull. Vet. Admin., 20: 287 (Jan.) 1914.

Heart Disease Therapy: Dramatic response was obtained in rheumatic fever. Adult dose was 40 mgm. intravenously, followed every six hours by 20 mgm. for several days, then 10 mgm. daily. Recovery in one month with total of 430 mgm. Child was given 10 mgm. intravenously, repeated next day. Also high vitamin diet and oral vitamin B complex. Morehead, Northwest Med., 41: 65 (Feb.) 1942. A case was treated with 100 mgm. and 1 ml. vitamin B complex per day, given intramuscularly. Freedberg and Blumgart, New England J. Med., 229: 939 (Dec.) 1913.

Myocardial Dysfunction Therapy: 10 to 60 mgm. was given parenterally, daily, and after acute symptoms were over, 3 mgm. three times a day. Eustis, New Orleans M. & S. J., 91: 369 (Feb.) 1912.

"Dry Socket" Therapy: Intramuscularly, 1 ml. relieved pain in 69% of 130 cases in 20 to 30 minutes. If pain had been present for two or more days, injection was repeated within 20 minutes, which brought relief in all but five of 130. Prophylaxis: Orally, 5 mgm. for three days preoperatively and 100 mgm. injected one hour or more before operation. Osterloh, J. Am. Dent. A., 39: 1445 (Aug.) 1912.

Herpes Zoster: Subcutaneously, 5 to 10 mgm. daily for six to seven days relieved pain and healed lesions rapidly. Edgerton, Arch. Ophth., 31: 114 (Aug.) 1915.

Dermatology: Six to 50 mgm. daily had variable effect upon actodinia, was of value in individual cases of tabetic pain, and had questionable

value in herpes zoster. Novy, California & West. Med., 56: 144 (Mar.) 1942.

Delirium Tremens: Intravenous injection of 50 ml. 50% dextrose, 8 ml. thiamine (25,000 units) and 25 units insulin simultaneously was successful in 15 patients. Cannon et al., J.A.M.A., 119: 1418; 1942.

Retrobulbar Neuritis Therapy: Intramuscularly, 10 to 40 mgm. for a total of 140 to 500 mgm. Clark, South. M. J., 35: 489 (May) 1942.

Seasickness and Airsickness: At least 15 mgm. per day should be given beginning two days before sailing or flying. Intramuscular injection of 50 mgm. given to combat airsickness. Holmes, Ohio State M. J., 40: 237 (Mar.) 1944.

Migraine Therapy: Intramuscularly, 100 mgm. per day, orally, 50 mgm. nicotinic acid three times a day and 15 ml. vitamin B complex twice a day were given for those experiencing more than ten days of headache in a month. Palmer, Clinics, 4: 531 (Aug.) 1945.

Prophylactic dose was 30 to 100 mgm. intramuscularly, daily. 23 of 48 were relieved and 14 of 48 had reduced frequency. 120 to 180 mgm. injected for acute attack. Palmer, Arch. Neurol. & Psychiat., 45: 368 (Feb.) 1941.

25 mgm. twice a day parenterally, for ten days and then 10 mgm. twice a day orally freed migraine in one case. Weinstein, J. Tennessee M. A., 35: 458 (Dec.) 1942.

Tabetic Lightning Pain: Intravenously, 100 mgm. daily for one week, then semi-weekly. Average amount was 1098 mgm. in 18 doses over eight months given to 26 tabetic patients with relief in some. Cocherms and Kemp, Am. J. Syph., Gonorr. & Ven. Dis., 26: 574 (Sept.) 1942.

Thiamine Content per 100 gm. in 34 normal pregnant, eight with hypertension, two with edema, seven with pre-eclampsia, and five with eclampsia was 19.4, 19.8, 32.2, 21.3 and 5.9 international units, respectively. Nixon, Wright, and Fieller, Brit. M. J., I: 605 (May) 1942.

Uveoparotitis Therapy: 30 mgm. daily produced cure in three months. Harper, North Carolina M. J., 6: 448 (Oct.) 1945.

Muscular Fatigue: More than 0.3 mgm/1000 calories intake had no effect on muscular work and fatigue in normal individual. Henschel, Minnesota Med., 25: 974 (Dec.) 1942.

Parenteral Use Dosage ranged from 3 mgm. daily for those unable to take food orally, but had been in a good nutritional state previously to 10 mgm. daily for those whose stores were depleted but had no sign of deficiency. Ingelfinger, New England J. Med., 233: 379 (Sept.) 1945.

Overdosage: Two cases with toxic reactions followed 10 and 17 mgm. daily intake for over two weeks. Headache, increased irritability, insomnia, rapid pulse, weakness and trembling were observed. Mills, J.A.M.A., 116: 2101; 1941.

Clearance Test: Parenterally, 350 micrograms per square meter of body area caused excretion within four hours of 50 micrograms for normals, and less for deficient individuals Melnick and Field, J. Nutrition, 24: 131 (Aug.) 1942.

Thiochrome Test showed that oral 3 mgm led to body saturation. McAlpine and Hills, Quart. J. Med., 10 31 (Jan.) 1941.

THIAMINE HYDROIODIDE

Rats—

Antineuritic Potency: 7.7 and 5 micrograms in aqueous solution injected daily had antineuritic potency as high as thiamine hydrochloride. Tolpin et al., J. Am. Chem. Soc., 63 2848; 1941.

THIOBARBITAL

(5,5-diethylthiobarbituric acid)

Man—

Graves' Disease: 0.025 to 1 gm daily given to 23 patients gave good clinical results in 23; eight who obtained complete remission showed no relapse on withdrawal of drug. Astwood, J Clin. Endocrinol., 5: 345 (Oct.) 1945.

Hyperthyroidism Therapy: 100 mgm daily was effective dose. It was more than three times as active as thiouracil, and more prolonged in action. Toxicity shown were drug fever in four of 30, muscle pains, and fatal agranulocytosis in one. Astwood, Bull New England M. Center, 7: 202 (Oct.) 1945.

Orally, 0.05 to 0.2 gm. daily gave prompt response in 28 cases. Toxic reactions occurred in 28%, therefore, it should be given only to patients unable to tolerate thiouracil. Bartels, J A.M.A., 129 932 (Dec) 1945.

Toxic Reactions: Drowsiness was observed after 0.3 to 1 gm. per day; drug fever with profound malaise from fifth to eighth day of therapy; mild headache and lassitude were seen. Astwood, J Clin Endocrinol., 5: 345 (Oct.) 1945.

THIOCYANACETATE

(Isobornyl)

Rats, Guinea Pigs, Rabbits—

Toxicity: Lotion was nontoxic orally or in vapor. Shelanski et al., Arch. Dermat. & Syph., 51: 179 (Mar) 1945.

Man—

Pediculosis: One application of emulsion containing 5% and 0.6% dioctyl sodium sulfasuccinate eradicated pediculus capitis infestation in 90% of 1487; remainder required no more than two applications. Ibid.

Toxicity: 200 exposed to fine spray of 5% solution half an hour per day for five days and similar exposure for three days after three week rest period showed no harmful effect. Ibid.

THIOURACIL**Tadpoles—**

Metamorphosis Inhibition: 1:2000 concentration inhibited metamorphosis of *R. clamitans* ordinarily induced by injection of thyrotropin. Hughes and Astwood, *Endocrinology*, 34: 138 (Feb.) 1944.

Capons and Cockerels—

Plumage Changes as in thyroidectomy after 0.3 to 0.5 gm. daily for 24 to 28 days; maintained approximately 18 to 20 days beyond cessation of medication. Domm and Blivaiss, *Proc. Soc. Exper. Biol. & Med.*, 57: 367 (Dec.) 1944.

Chicks (White Plymouth Rock)—

Thyroid Enlargement: Maximal enlargement expressed as thyroid weight in mgm/100 gm. body weight was secured in about 12 days when 0.1% thiouracil was fed in diet. Females exhibited greater thyroid response than males Mixner, Reinecke, and Turner, *Endocrinology*, 34: 168 (Mar.) 1944.

Rats (castrated)—

Mammary Glands: Subcutaneously, 10 mgm/100 gm. per day or 0.1% in drinking water for 18 to 35 days caused hyperplasia of thyroid and reduced growth. When 0.05 mgm. α -estradiol dipropionate was also given last ten days, marked lobule alveolar development appeared. When 0.005 mgm thyroxin was given concurrently, hyperplasia of thyroid was reduced and lobule alveolar growth of glands disappeared. Smithcors, *Proc Soc. Exper. Biol. & Med.*, 59: 197 (June) 1945.

Rats (male and female)—

Chronic Poisoning: 40 to 120 mgm. daily for 14 to 385 days showed irregular progressive increase in adrenal medulla. Marine and Baumann, *Am. J. Physiol.*, 144. 69 (June) 1945.

Rats—

Metabolism: 200 to 250 mgm/kg. per day depressed basal metabolic rate an average of 12% by 24th day with no further change in 94 days.

Thyrotrophin, producing a 24.8% increase in basal rate in normal animals, gave only +15.7% when injected into those treated with thiouracil for 14 to 21 days. Barker, *Endocrinology*, 37: 230 (Oct.) 1915.

Resistance: 0.2% in diet for three weeks before exposure, or injection of 15 mgm. dilantin sodium, intraperitoneally one and a half hours before exposure, or more markedly, by combining both, survival time of rats at low barometric pressure (148 mm. Hg equivalent to altitude of 39,000 feet) was prolonged. Gordon, Goldsmith, and Charipper, *Proc. Soc. Exper. Biol. & Med.*, 56: 202 (June) 1914.

Effect: 0.2% in food, administered for 19 to 15 days caused marked thyroid hyperplasia and basophilia, increased resistance of animals to lowered barometric pressure (190 mm Hg), inhibited normal weight gains, and after 38 days induced slight anemia and granulocytopenia. Gordon, Goldsmith, and Charipper, *Endocrinology*, 37: 223 (Oct.) 1915.

Man—

Thyrototoxicosis: 200 mgm. three times a day at six hour intervals for one to two weeks followed by maintenance dose of 100 mgm. or less per day over three to 15 months improved 30 of 35 cases Watson, *J. Clin. Endocrinol.*, 5: 273 (July-Aug.) 1915.

Daily administration of two to eight tablets containing 0.2 to 0.8 gm. for two weeks to 16 months effected subjective improvement of 78 patients. McGavack, *J. Clin. Endocrinol.*, 5: 259, 1915

0.5 gm., twice a day until symptoms disappeared, followed by 0.2 gm., daily or twice a day, and then 0.05 to 0.19 gm., daily as maintenance dose. Improvement in 22 of 29. Grainger, Gregson, and Pemberton, *Brit. M. J.*, II: 313 (Sept.) 1915. 0.2 gm. five times daily for an average of 29.3 days caused average gain of 3.75 kg. in 22 patients and marked improvement in symptoms. Himsworth, *Proc. Roy. Soc. Med.*, 37: 693 (Oct.) 1914.

0.6 gm. daily later reduced to 0.1 or 0.3 gm. was successful in improving 16 of 19 patients. Montagne and Wilson, *West J. Surg.*, 53: 65 (Mar.) 1915.

0.8 gm. per day initially, gradually reduced to a maintenance dose of 0.1 to 0.3 gm. per day was effective in 19 of 20 Raveno, *J. Michigan M. Soc.*, 41: 276 (Mar.) 1915.

Maximum dose required was 200 mgm. daily or daily. Eaton, *Lancet*, I: 171 (Feb.) 1915.

0.4 to 0.6 gm. daily, followed by maintenance doses of 0.1 to 0.1 gm. daily for 2.5 to 6 months gave good results in eight of ten patients Sexton and Levy, *J. Missouri M. A.*, 12: 621 (Oct.) 1915.

Initially, 1 gm. three times a day followed by 0.2 gm. five times a day

for an average of 29 days was in general an unnecessarily high dosage. Now 0.5 gm. daily was reduced to maintenance dose of 0.1 to 0.05 gm. Three to four weeks treatment was not enough after previous iodine therapy. Himsworth et al., *Brit. M. J. I*: 852 (June) 1944.

Basal metabolic rates and corresponding dosages were: +40, 0.3 to 0.4 gm., three times a day; +20 to 30, 0.2 to 0.3 gm., three times a day; +10 to 20, 0.1 to 0.2 gm., twice a day. Maintenance dose was 0.1 to 0.2 gm., daily. Cannon, *J. M. Soc. New Jersey*, 41: 339 (Sept.) 1944.

Maintenance dose was 0.1 to 0.2 gm. reduced gradually from 1.0 gm. or 0.6 gm. (rarely 0.4 gm.) daily for a six week period. Williams and Clute, *New England J. Med.*, 230: 657 (June) 1944.

0.6 gm. daily decreased metabolic rate to normal or nearly normal in 11, and permitted subtotal thyroidectomy. Treatment required 20 days to six months. Bartels, *J.A.M.A.*, 125: 24; 1944.

0.3 to 1.0 gm. daily to 26 patients caused reduced basal metabolic rate and blood pressure, increased body weight, and often decreased size of thyroid. After reduction of basal metabolic rate, 0.2 to 0.4 gm. daily was sufficient for maintenance. Toxic reactions found in 16 among 135 cases of thiouracil therapy cases in literature. Minimal danger of toxic reactions and maximal effectiveness were obtained with 0.8 to 1.0 gm. daily for five to ten days when basal metabolic rate was +50 or over, 0.6 gm. when between +30 and +50, and 0.4 gm. otherwise. Subsequent maintenance dose should be 0.2 gm. McGavack et al., *J. Clin. Endocrinol.*, 4: 249 (July) 1944.

Graves' Disease: Patients on constant creatin, creatinine free diets receiving thiouracil showed improvement in all metabolic functions: creatinuria sharply reduced, creatin tolerance after 1.32 gm. creatin rose rapidly and remained normal; sugar tolerance tests were normal; nitrogen, phosphorus and calcium balances became progressively positive. With 1 gm. thiouracil in 24 hours, serum cholesterol rose to myxedematous levels. Sloan and Shorr, *Science*, 99: 305 (Apr. 14) 1944.

Orally, 0.6 gm. per day at first, and reduced to 0.4 gm. per day after basal metabolic rate dropped half way to normal. Administered ten to 36 days before thyroidectomy. Thyroglobulin from gland contained one-fourth to one-third amount of iodine expected in normals or those of thyrotoxic iodine treated patients. Rawson et al., *J. Clin. Endocrinol.*, 4: 1 (Jan.) 1944.

Preoperative Therapy: 0.6 gm. daily in three doses for six, and thiouracil and 1.5 ml. of Lugol's solution were given to 25 patients. Basal metabolic rate before therapy was +55, after 26 days' treatment +18, and

five to ten days after operation +9 Newman, M. Clin North America, 29: 302 (Mar.) 1915.

Angina Pectoris: 0.4 gm. daily in divided doses gradually reduced to 0.1 gm. daily obtained decrease in number or complete disappearance in angina attack in seven out of ten Raab, J. A. M. A., 128: 249, 1915.

Distribution and Excretion Rapidly absorbed from gastrointestinal tract and readily excreted in urine. Blood concentration of 0.8 to 6.4 mgm % with doses of 0.2 to 1.2 gm. daily, while excretion varied from 16 to 618 mgm. Most of thiouracil in blood was in red blood cells. At autopsy drug was found in all tissues. Destroyed by contents of stomach and small intestines. Rapidly destroyed by tissues of body, none excreted in stool. Williams, Kay, and Jandorf. J Clin Investigation, 23: 613 (Sept.) 1944.

Metabolic Effect (adrenal function) One gram daily for two to five weeks caused in some patients, retention of sodium, chlorides and nitrogen, creatinine and creatine. One patient with Cushing's disease showed marked drop in 17 ketosteroid excretion. Williams et al., J Clin Endocrinol., 4: 58 (Feb.) 1914.

Toxicity: Danger of agranulocytosis, so leucocyte count was necessary every two to three days in every patient 1 gm. daily for three days, then 0.6 gm. daily until basal metabolic rate approached normal, then a maintenance dose of 0.2 gm. was given Granulopenia appeared suddenly in 20% of patients. In some, sudden rise in temperature accompanied by arthralgia, myalgia, lymphadenopathy or appearance of rash. Exophthalmos increased in none and improved in one patient Fishberg and Vorzimer, J. A. M. A., 128: 915; 1915.

Fatal agranulocytosis with jaundice, drug fever, accompanied by splenomegaly and monocytosis. Submaxillary gland swelling occurred in two; leukopenia, neutropenia and urticarial dermatitis in one patient. Gargill and Lesses, J. A. M. A., 127: 890; 1915

Agranulocytosis: 19 gm. was given in 10 days in daily doses of 400 to 600 mgm. Another patient given 22 gm. in seven weeks caused basal metabolic rate to fall from +12% to -5% and resulted in delusional insanity. Pearson, Lancet, 219: 9 (July) 1915.

0.6 gm. was given daily for 31 days, 0.1 gm. daily for 11 days, 0.2 gm. for 21 days; and 0.1 gm. for ten days resulted in fatal agranulocytosis Wosika and Braun, J. Lab. & Clin Med. 30 779 (Sept) 1915

Epinephrine Sensitivity: 0.2 gm. twice a day for three months weakened electrocardiographic response to epinephrine and diminished heart rate acceleration. Raab, J. Lab. & Clin Med., 30 771 (Sept) 1915

Mental Confusion: 22.4 gm. taken in two months caused confusion lasting for two weeks. Atkin, Lancet, 249: 562 (Nov.) 1945.

Fatality: 70 year old man was given 0.2 gm. four times a day for three days, 0.3 gm. four times a day for 128 days, and 0.9 gm. daily for 29 days, later cut to 0.6 gm. daily. Seven days later, white cell count was 1,250. Pharyngitis developed, white cell count dropped to 450. Patient died despite intramuscular injection of nucleotide, blood transfusion and penicillin. Hemoglobin casts found in renal tubules. Ferrer, Spain, and Cathcart, J.A.M.A., 127: 646; 1945.

Fatal Agranulocytosis: Resulted from 30.8 gm. given in 54 days. Kahn and Stock, J.A.M.A., 126: 358; 1944.

Sensitivity: Fever and rash in one, and fever in three of nine patients treated with 1.0 gm. per day for eight to 16 days for hyperthyroidism. Gabrilove and Kert, J.A.M.A., 124: 504 (Apr. 14) 1944.

THIOUREA

Rats (adult, males)—

Granulocytopenia: Addition of 0.5% to standard diet caused neutrophilic agranulocytopenia. Neutrophils dropped from 32.7% to 7% after 40 days and to 5.4% after 58 days on this diet. 5% solubilized liver prevented this, therefore use of liver and cholic acid was suggested for prevention. Goldsmith et al., J.A.M.A., 125: 847; 1944.

Rats—

Electrocardiographic Changes: 1% in drinking water for three weeks slowed heart rate to two-thirds of original value, increased conduction time, and caused weight loss. Waller and Charipper, Am. J. M. Sc., 210: 443 (Oct.) 1945.

Exposure to Low Atmospheric Pressure: of 200 mm. Hg for two hours caused no mortality in female rats fed 0.5% thiourea for 12 to 30 days, 50% for those fed four to eight days, 60% for those injected 200 mgm. in water five hours before exposure, and 75% for no treatment. Gordon, Goldsmith, and Charipper, Science, 99: 104 (Feb. 4) 1944.

Iodine Metabolism: 1% in diet for two months prevented conversion of inorganic iodide to organic iodide by thyroid. Keston, J. Biol. Chem., 152: 241 (Feb.) 1944.

Pulmonary Edema 5 mgm. added to diet caused fatal pulmonary edema in less than 16 hours in five month old rats. Autopsies showed 7 to 15 ml. serous fluid in pleural cavity. Intraperitoneally or orally, 18 mgm. killed young adult rats in two hours. Intraperitoneally, 180 mgm. to

immature rats (1.0 to 1.5 months) did not cause death. Mackenzie and Mackenzie, *Proc. Soc. Exper. Biol. & Med.*, 54: 31 (Oct.) 1913.

Man—

Granulopenia and Thrombopenia resulted in a patient given 1 gm. three times a day for ten days, then twice a day for one week, then daily. Treatment consisted of transfusion of 500 ml. whole, fresh blood, and administration of 10 ml. pentnucleotide three times a day (discontinued after six doses due to pyrexia). Newcomb and Deane, *Lancet*, 216: 179 (Feb.) 1944.

Thyrototoxicosis: Symptoms disappeared in eight days with 0.5 to 5.0 gm. per day and subsequent maintenance dose of 0.25 to 2 gm. per day. Enlargement of thyroid was not reduced in all cases, but tremor, tachycardia, and myasthenia were abolished. Basal metabolic rate and blood cholesterol levels returned to normal, and lost weight regained, exophthalmic eyes became normal in three. Nausea usually followed administration, characteristic breath and urine odors. Other effects were maculopapular rash, intermittent watering of eyes, fever and granulopenia. Ritchie and Geddes, *M. J. Australia*, 31: 381 (Apr.) 1911.

THORIUM DIOXIDE, COLLOIDAL (Thorotrast)

Man—

Diagnostic Advantages There was no instance of proved liver damage since its introduction 14 years ago. Four cases were given intravenous injections to facilitate X-ray search for tumors, cirrhosis, duct obstruction, gumma, and size variation in liver and spleen. A man was still alive ten years after three daily doses of 25 ml. McClure, Jankelson, and Osgood, *Rev. Gastroenterol.*, 11: 17, 1911.

THYMOL

Mice (white)—

Experimental Histoplasmosis Intraperitoneally, 1 mgm. in olive oil starting 24 hours after infection was unsuccessful. Levy, *Am. J. Trop. Med.*, 25: 241 (May) 1915.

Guinea Pigs—

Tuberculosis Prevention 1 gm. kg. daily in olive oil caused 70% to survive 15 weeks after tuberculosis (human) inoculation, 50% survived 20 weeks, and 20% survived 28 weeks. All controls died. McBurney et al., *J. Lab. & Clin. Med.*, 30: 32 (Jan.) 1915.

THYMOXYETHYLDIETHYLAMINE

Rats—

Histamine Antagonist: Subcutaneously, 40 mgm/kg. protected against two lethal doses of histamine administered previously. Climenko, Hom-burger, and Messer, J. Lab. & Clin. Med., 27: 289 (Dec.) 1941.

Guinea Pigs—

Toxicity: There was no death in three given 15 mgm/kg., intrave-nously; two out of three died with 16.5 mgm/kg. Ibid.

Cats—

Effect: Intravenously, 4 mgm/kg. under anesthesia slowed respiratory rhythm and diminished amplitude of respiration followed by fall of blood pressure, apnea, and heart failure. Subcutaneously, 10 mgm/kg. to anesthetized cat had no apparent effect. Ibid.

THYMUS HORMONE

Guinea Pigs—

Relation to Thyroid: Thymus administration increased normal weight of thyroid of below 30 mgm. to over 40 mgm., highest being 45 mgm. Bomskov and Spiegel, Endokrinologie, 23: 225; 1941.

THYROID

Rats—

Ovarian Development: On diets containing 0, 0.5 and 1.0% desiccated thyroid, female rats were raised to maturity, but ovarian development was inhibited, remaining infertile both in weight and histologic appear-ance. Ershoff, Endocrinology, 37: 218 (Sept.) 1945.

Guinea Pigs—

Histamine Sensitivity: Orally, five doses of 0.02 gm. thyroid extract per 100 gm. given over five to six day period rendered animals more sensitive to histamine shock. Farmer and Fribourg, Proc. Soc. Exper. Biol. & Med., 50: 208 (June) 1942.

Man—

Cretinism: Dosages were: 0.0065 to 0.48 gm. for infants; 0.032 to 0.097 gm. for children two to four years, 0.065 to 0.191 gm. for children four to twelve years. Drug administered without interruption through life. De Court, Rev. clin. de São Paulo, 10: 125; 1941; through J.A.M.A., 118: 1336; 1942.

Myxedema: 30 mgm per day increased to 120 mgm. for seven weeks caused rise of basal metabolic rate from -38% to -4% and blood chole-

terol level dropped from 667 mgm.% to 191 mgm.%. In another patient given 30 mgm. a day increased gradually to 100 mgm. caused rise of basal rate from -35% to $+8\%$ and blood cholesterol dropped to 196 mgm.% from 926 mgm.% in three months. Craig Lissak, and Soley, J. Clin. Endocrinol., 4: 12 (Jan) 1914.

Prolonged Use: Medication for three cretins started in 1907 with 0.3 gm. daily and increased to 2.2 to 3.2 gm. In 1911 they were normal and still taking as much as 3.2 gm. daily. In 1911, they were taking $\frac{1}{2}$ gm. three times a day, were well, had no tremors or tachycardia. Block, Diseases of Nervous System, 3: 213 (July) 1912.

Recurrent Hyperthyroidism was prevented by 30 mgm. extract twice a day after all thyroidectomies over a period of one year. De Courcy, Ohio State M. J., 38: 449 (May) 1912.

Serum Iodine: 60 mgm. increase in daily dose given to hypothyroid subjects caused an increase of 2.0 gammas % serum iodine. Within limits of 0 and 120 mgm. per day, relationship between serum iodine and thyroid dose appeared to be linear. Winkler, Riggs and Man. J. Clin. Investigation, 24: 732 (Sept.) 1915.

More than 0.6 gm. to patients elevated basal metabolic rate and serum iodine level abnormally, and decreased serum cholesterol and protein levels. Riggs, Man, and Winkler, J. Clin. Investigation, 21: 722 (Sept.) 1915.

THYROXIN

Mice (virgin females)—

Growth and Food Intake. Subcutaneously, 0.015 to 0.01 mgm. crystalline thyroxin caused mice (13 to 16 gm.) to gain 28% more than controls in five weeks, and food intake was 25% above controls. Koger, Hurst, and Turner, Endocrinology, 31: 237 (Aug) 1912.

Rats—

Cardiac Action: Thyroidectomy decreased heart rate from 431 to 339 beats per minute in fully conscious restrained animals and from 379 to 265 beats per minute in anesthetized animals. 3 micrograms thyroxin daily restored heart rate almost to normal. 50, 300 and 5000 micrograms gave values above normal, reaching for highest dose 617 in conscious and 571 for nembutal treated rats. Ichlund and Hoff, Am. J. Physiol., 111: 32 (Mar.) 1914.

Hemopoiesis: Intramuscularly, 1 mgm. to 12 adult animals every two or three days caused no significant change in blood but number of myelocytes and eosinophile cells of marrow were decreased. Wilson. M. J. Australia, 31: 261 (Mar.) 1911.

Dogs—

Galactose Absorption: Intramuscularly, 0.5 mgm/kg. daily for 22 days caused rapid absorption from intestinal tract during first week, and delay in clearing blood of galactose occurred later. Grauer et al., *Endocrinology*, 30: 474 (Mar.) 1942.

TOCOPHEROL, ALPHA**Mice—**

Reproduction Requirement: 0.5 to 1.0 mgm. at beginning of gestation permitted birth of young to 85%. Goettsch, *J. Nutrition*, 23: 513 (Mar.) 1942.

Rats—

Prophylactic Requirement: 0.25 mgm., six times weekly was borderline dose with dystrophy in young; 0.75 mgm., six times weekly was adequate. Emerson and Evans, *J. Nutrition*, 21: 5; 1941.

Protracted Effect of single dose: Administration of 0.5 to 1.0 mgm. d,l-alpha tocopherol acetate to 15 day old males of vitamin E deficient rats delayed post-pubertal testicular degeneration and retarded its course. Administration of 5 mgm. on 15th day was more effective. 1 mgm. dose on 29th and 30th day was less effective than on 15th but on sixth and eighth days was totally ineffective. Kaunitz, Pappenheimer, and Schogoleff, *Am. J. Path.*, 20: 247 (Mar.) 1944.

Reproduction Requirement: 2.5 mgm. fed at beginning of gestation permitted birth of young to 85%. Goettsch and Pappenheimer, *J. Nutrition*, 22: 463 (Nov.) 1941.

Muscular Dystrophy Prevention: 0.5 mgm. fed on 15th and 17th day of lactation prevented dystrophy in 85%. *Ibid.*

Requirement: 0.75 mgm. daily required for normal growth and reproduction. Evans and Emerson, *J. Nutrition*, 22: 555 (Dec.) 1943.

Guinea Pigs—

Muscular Dystrophy and Pregnancy: Diet supplemented by weekly doses of 5 to 10 mgm. prevented resorption of embryo and muscular dystrophy. Pappenheimer and Goettsch, *Proc. Soc. Exper. Biol. & Med.*, 47: 268 (June) 1941.

Rabbits—

Dystrophy: Orally, 20 mgm caused disappearance of physical symptoms in seven days and growth response within two days. 20 mgm. parenterally prolonged life and maintained weight. 100 to 200 mgm., intramuscularly or subcutaneously produced slow response in some, pro-

longed life and promoted growth in others, though outcome was fatal. Mackenzie and McCollum, *Proc. Soc. Exper. Biol. & Med.*, 48: 642 (Dec.) 1941.

Nutritional Muscular Dystrophy treated with 5 to 15 mgm. for first three attacks, 20 to 40 mgm. for subsequent attacks. MacKenzie, *Proc. Soc. Exper. Biol. & Med.*, 49: 313; 1942.

TOCOPHEROL, ALPHA QUINONE

Mice (pregnant)—

Action: Orally, 100 mgm. d,l-alpha tocopherol quinone daily caused rapid loss of weight and after three weeks extensive vaginal bleeding. Intraperitoneally, 400 mgm. was more active and produced comparable results. Effects prevented by simultaneous administration of menadione in olive oil. Woolley, *J. Biol. Chem.*, 159: 59 (June) 1945.

TOCOPHEROLS

Man—

Fibrositis Therapy: Orally, 0.6 ml daily of concentrated preparation of natural mixed tocopherols. Steinberg, *New York State J. Med.*, 42: 773 (Apr.) 1942.

TOLUENE

Man—

Poisoning: 1% of those exposed to more than 500 parts per million revealed symptoms of nausea, headache, anorexia, palpitation, extreme weakness, and loss of coordination. Red blood cells dropped to 2.5 million per ml. and in two instances, leukopenia. Treatment consisted of 250 ml. of whole blood for bone marrow degeneration; 10 mgm. liver intramuscularly daily, daily doses liver, orally; iron, calcium, phosphorus, yellow bone marrow, multiple vitamin, 400 to 600 mgm ascorbic acid per day, orally; high vitamin high caloric diet. Exposure to fumes in concentration of less than 200 parts per million was not hazardous. Wilson, *J.A.M.A.*, 123: 1106; 1943.

Toxicity: 200 parts per million exposure for eight hours caused impairment of coordination and reaction time. Higher concentrations were damaging in three hours. Von Ottingen et al, *Science News Letter*, 40: 239; 1941.

TRIAZOLE DERIVATIVES

Rats—

Pharmacology: 1-phenyl-1,2,3-triazole 4-carboxylic acid-dimethyl and diethyl derivatives reduced temperature 2° C. below normal in yeast

treated rats, rising to normal in five hours. Sodium salts were less effective. 100 mgm. di-isobutyl and aminoethyl ester triazoles were without antipyretic action. Sodium salt and dimethyl and diethyl amides had more powerful analgesic action than other members of the series, but diethyl derivative was only one with definite analgesia without marked toxic effects. There was no advantage over aminopyrine. Cunningham, Fellows, and Livingston, *J. Pharmacol. & Exper. Therap.*, 73: 312 (Nov.) 1941.

TRIBROMETHANOL

(Avertin)

Rabbits—

Rectal Administration: Delayed deaths in 35 of 89 animals antidoted with picrotoxin and given sub-lethal or lethal doses rectally. This was caused by rectal irritation and perforation of intestine. Solution contained 1 gm. avertin crystals plus 0.5 ml. amylene hydrate. Maloney, *J. Pharmacol. & Exper. Therap.*, 75: 247 (July) 1942.

Man—

Poisoning (child, 8 years): 80 mgm/kg. caused death from acute yellow atrophy of liver and uremia. Andersen, *Anesthesiology*, 6: 284 (May) 1945.

TRICHLOROBENZENE

Rats—

Toxicity: Repeated exposure to 0.2 to 0.3 mgm. per liter produced vascular and nervous system changes; also leucocytosis followed by leucopenia. Rozanova, *Farmakol., Toksikol.*, 6: 48; 1943.

TRICHLORETHYLENE

(Trilene)

Rats—

Toxicity: Three animals exposed to trilene-dichloroacetylene mixture for 30 minutes died in convulsions. Rats exposed to trilene alone recovered. Dichloroacetylene was only substance found in quantity when trichlorethylene was passed over soda-lime. Hunter, *Brit. M. J.*, 1: 34 (Mar.) 1944.

Man—

Untoward Effects: Inhalation of 1.5 gm. (1 ml.) to relieve headache produced syncope, transient cardiac arrhythmia, pulse acceleration. Geiger, *J.A.M.A.*, 123: 141; 1943.

Serious disorders of cardiac function; an increase in vagal tone and

irritability of vagal reflexes; convulsions leaving drowsiness or mental confusion for some hours later: fifth nerve sensory loss Hunter, *Lancet*, 246: 308 (Mar.) 1944.

Cardiac irregularities and excessive bleeding developed in 16% of 500 patients, ten or more minutes after trichlorethylene (trilene) and nitrous oxide plus oxygen anesthesia from a standard Boyle machine was begun. Johnson, *Lancet*, 246: 357 (Mar) 1944.

Anesthesia induced with 0.8 gm. pentothal intravenously and maintained by gas and oxygen passed over 60 ml. of trilene. Symptoms of liver damage appeared on fourth postoperative day and death resulted from acute yellow necrosis. Herdman, Brit. M. J., II 689 (Nov.) 1915.

Poisoning: Orally, 15 ml. caused dizziness, numbness of limbs, deafness, incontinence, and amnesia. Recovery. Naish, Brit M J., II: 367 (Sept.) 1945. Toxic symptoms resulted after drinking 15 ml and 16 ml. respectively, and recovery in five and ten days, respectively. Stephens, Brit. M. J., II: 218 (Aug.) 1945.

All cases reported in literature (1931-1941) of occupational exposure to petroleum solvents and trichlorethylene were given in detail as to length of exposure, symptoms, length of illness, etc. Quadland, *Indust. Med.*, 13: 45 (Jan.) 1944.

TRICHLORETHANE

Man—

Poisoning: Death from inhaling through cigarette was due to decomposition of gas as it passed through cigarette Derrick, M. J. Australia, 30. 355 (Oct.) 1943.

TRICHOPHYTIN

Man—

Dermatophytoses: Desensitization with subcutaneous injection of 1:100,000 mixed trichophytin solution twice weekly gradually increased to 0.5 ml. of 1:100 dilution, together with proper therapy resulted in cure of 53, control of mycosis in 38, and failure in four Schonwald, Ann. Allergy, 2: 10 (Jan.-Feb.) 1914.

TRIDIONE

(3,5,5-trimethyl-2,4-oxazolidine-dione)

Man—

Epil
bital. I

ed or greatly reduced number of psychomotor seizures. De Jong, J.A.M.A., 130: 565; 1946.

TRIETHANOLAMINE

Bacteria—

Aerial Disinfection: 150 mgm/cubic meter of air was bactericidal for airborne organisms in sprayed saliva at 70% humidity and 60–70° F. Lovelock, Lidwell, and Raymond, Nature, 153: 20; 1944.

TRIETHYLENE GLYCOL

Bacteria—

Air Contaminants: Hemolytic streptococci were completely eliminated by vapor concentration of 0.0025 to 0.004 mgm/liter air for six weeks. All airborne infections reduced by 12%. Bigg et al., Proc. Cent. Soc. Clin. Research, 17: 38; 1944.

TRIMETHYL AMMONIUM SALTS

Mice—

LD₅₀: Intraperitoneally, phenyl compounds, mM/kg. I, 0.15; II, 0.065; phenyl propyl, 0.035; phenbutyl, 0.09; phenyl amyl, 0.10; B-methyl phenyl, 0.3; phenallyl, 0.07; alpha methyl phenmethyl, 0.15; alpha methyl phenethyl, 0.10; alpha methyl phenpropyl, 0.08. Alles, Univ. California Publ. in Pharmacol., 2: 161 (Mar.) 1944.

TRIORTHOCRESYL PHOSPHATE

Mice—

Acute Toxicity: Minimal lethal dose was 0.28 ml/kg. for average mouse. Hodge and Sterner, J. Pharmacol. & Exper. Therap., 79: 225 (Nov.) 1943.

Dogs—

Skin Absorption: Urinary excretion was 0.1% of dose applied on skin. Retention in tissues was in following order: visceral organs, muscle, brain, and bone. Ibid.

Man—

Skin Absorption: 8 micrograms per 100 ml. blood level in 24 hours, and urinary excretion was 0.1 and 0.4% of dose applied to skin in two cases. Ibid.

TRIPHENYLCHLOROETHYLENE

Man—

Inhibition of Lactation: Orally, 0.5 gm. three times a day for four days, and then 0.5 gm. daily for rest of week. Moir, Brit. M. J., I: 681; 1942.

TRYPARSAMIDE**Man—**

Optic Nerve impaired in 3 to 4% of patients following 1.0 to 3.0 gm., intravenous injection within 24 to 48 hours after one of first ten injections. Treated with intramuscular injection of thiamine, 10 mgm. daily, plus oral vitamin B complex preparation, and intravenously 1.0 gm. of sodium thiosulfate. Buley and Albers, *Illinois M. J.*, 81: 477 (June) 1942.

Trypanosomiasis: Intravenously, 6 to 8 gm. daily for six to 12 days made 35 of 42 symptom free. Adults were given 2 gm. per 40 to 50 kg. in 1 liter of distilled water, by continuous intravenous drip at 40 drops per minute for eight hours daily for six days or eight to 12 days with one day rest interval, after three to four treatments. Fowler, *Tr. Roy. Soc. Trop. Med. & Hyg.*, 38: 297 (Mar.) 1945.

L-TRYPTOPHANE**Man—**

Urine Content: 12 to 30 mgm. daily secreted by normal male subjects. Schweigert, Sauberlich, and Elvehjem, *Science*, 102: 275 (Sept. 14) 1945

TUBERCLE BACILLI**Guinea Pigs—**

Immunity: Subcutaneously, 0 000,001 mgm. to 1 mgm. in graded amounts of human tubercle bacilli of low virulence protected against organ tuberculosis following injection of 1.0 mgm. of viable bacilli, while produced by 0 001 and occasionally 0 000,001 mgm. amounts in unprotected animals. Corper and Cohn, *Yale J Biol & Med*, 16: 333 (Mar.) 1944.

TUBERCLE ENDOTOXOID**Man (Bantu natives)—**

Tuberculosis Therapy: Subcutaneously, twice weekly beginning with 0.05 ml. first week; 0.1 ml. second, then increased 0.1 ml. per week to a maximum of 2.0 ml. This dose was repeated once or twice a week for several months as required. Caused immediate stabilization of weight and subsequent increase, decline and disappearance of night sweats, minimized coughing attacks, and reduced temperature to normal. Reduction in amount of sputum occurred and disappearance of *M. tuberculosis* and changes from acute to chronic infection with gradual clearing of pulmonary lesion. Grasset, *Am. Rev. Tuberc.*, 49: 1 (Jan.) 1944.

TUBERCULIN

Man—

Comparative Tests: 177 non-tuberculous skin disease patients and 23 tuberculoderms were tested. Agreement between reactions to 0.1 mgm. old tuberculin, intradermally and to undiluted old tuberculin as patch test was 85% and between 0.02 mgm. old tuberculin, intradermally and Vollmer patch test was 92%. Pascher and Sulzberger, Arch. Dermat. & Syph., 49: 256 (Apr.) 1914.

M. TUBERCULOSIS POLYSACCHARIDE

Man—

Reaction: Intracutaneously, 0.001 to 0.3 mgm. elicited in 67 patients skin reactions correlated in degree to extent of tuberculous involvement. Skin reactions were accompanied by rise in lymphocytes, fall in monocytes, and shift to right of Schilling index. At least 12 injections weekly elicited in tuberculous patients antibody capable of protecting guinea pigs against lethal doses of polysaccharide (20 mgm./ml. of normal saline for animals with generalized tuberculosis). Kropp and Foley, J. Lab. & Clin. Med., 29: 231 (Mar.) 1914.

TYPHOID PYROGEN

Rabbits—

Dosages: Maximum pyrogenic dose was 0.06 microgram/kg. Minimal lethal dose was 190 micrograms/kg. Co Tui, J. Am. Pharm. A. (Scient. Ed.), 5: 60 (Mar.) 1914.

Minimal pyrogenic dose was 0.06 microgram/kg. Minimal lethal dose was 175 to 190 micrograms/kg. Note: Minimal pyrogenic dose was intravenous dose which caused rise in temperature of 0.5 to 0.6° C. within four hours. Co Tui et al., J. Lab. & Clin. Med., 29: 58 (Jan.) 1914.

Dogs—

Minimal Pyrogenic Dose was 0.24 microgram/kg. Ibid.

Man—

Effect: 15 micrograms/kg. (750 times minimal pyrogenic dose) given to female patient of 78.6 kg. caused rectal temperature to rise from 37.5° to 40° C. within one hour 15 minutes and to 40.9° C. in six hours, pulse rate was 140; white blood cells dropped from 10,300 to 6,200 per cu. mm. blood. Patient vomited, became incontinent and unconscious for 48 hours with return to normal in 72 hours. Ibid.

Dosages: Minimal pyrogenic dose was 0.02 microgram/kg. Ibid.

Maximal pyrogenic dose was 0.06 microgram/kg. Minimal lethal dose was 190 micrograms/kg. Co Tui, J. Am. Pharm. A. (Scient. Ed.), 5: 60 (Mar.) 1944.

TYPHOID VACCINE

Man—

New Vaccine: 75% alcohol-killed and 25% alcohol preserved typhoid vaccine adopted by British Army contained full complement of V_1 antigen and probably induced antibody response superior to that of old heat-killed carbol-saline vaccine. Dose for men was 0.25 ml. followed by 0.5 ml. two weeks later; dose for women was 0.2 ml. and 0.4 ml.; annual reinoculation with 0.25 ml. recommended for both. Lancet, 216: 318; 1944.

Pityriasis Rosea: Treated with standard typhoid vaccine, 50 to 150 million killed organisms, intramuscularly into left triceps. In 62.6% condition cleared or improved after single injection. Ebert and Otsuka, J.A.M.A., 123: 1036; 1943.

Protection (of children): Intradermal injection provided as much protection as subcutaneous injection of one tenth of dose required for latter, and was far less painful and uncomfortable. Kamp, Monthly Bull. Indiana State Bd. of Health, 47: 9 (Jan.) 1914.

Re-immunization: Intradermally, 0.1 ml. was used by United States Army, two years or more after first immunization. Queries and Minor Notes, J.A.M.A., 119: 763; 1912.

TYPHUS

Man—

Cardiac and Circulatory Disturbance in typhus was treated with Sympatol [p-hydroxy- α (methyl-aminomethyl)-benzyl alcohol], 1.0 to 2 ml. subcutaneously or intramuscularly, three to six times daily; oral adminis-

Klin. Wchnschr., 22: 1 (Jan) 1913, through Quart. Rev. Med., 1: 122 (Feb.) 1914.

TYPHUS ANTISERUM

Guinea Pigs—

Experimental Typhus Intra abdominally, 1 ml. freshly prepared 10% suspension of typhus diseased guinea pig brain was given. One to five

days later, subcutaneous injection of 0.5 ml. refined hyperimmune rabbit serum concentrate shortened febrile reaction and led to recovery. Wyckoff and Bohnel, Proc. Soc. Exper. Biol. & Med., 49: 712 (Apr.) 1942.

TYPHUS CONVALESCENT BLOOD

Man—

Typhus Therapy: Single transfusion of 200 ml. of convalescents' blood given at beginning of disease gave good therapeutic results to 50 patients. Pfeiffer and Gauserky, Klin. Wochnschr., 22: 481; 1943; through Brit. M. J. I: 292; 1944.

TYPHUS SERUM

Man—

Convalescent Serum: Intravenously, 125 ml. sterile serum obtained from 464 donors and pooled according to group, reduced mortality rate from 14.7 to 6.4% in 94 patients. Meyer, Ztschr. f. Immunitätsforsch. u. exper. Therap., 103: 169 (July) 1943; through Trop. Dis. Bull., 41: 115 (Feb.) 1944.

Typhus Therapy: Intravenously, 40 ml. of hyperimmune rabbit serum on sixth and seventh day of illness to one patient; intramuscularly, 40 ml. and intravenously, 40 ml. to six patients as soon as diagnosis was established, and intramuscularly, 40 ml. the next day brought recovery to all. Stevens, Lancet, 248: 106; 1945.

An initial intravenous injection, then intramuscularly, 2.0 ml. hyperimmune antityphus rabbit serum per kg. administered during first 72 hours of illness, followed by 0.5 ml. serum per kg. intramuscularly, 24 hours and again 48 hours later was beneficial to ten of 25 unvaccinated patients. Yeomans, Snyder, and Gilliam, J.A.M.A., 129: 19; 1945.

TYPHUS VACCINE

Guinea Pigs—

Typhus: A single 1.0 ml. alum-precipitated vaccine protected experimental infections in 68%, while only 37% were protected by non-precipitated vaccine. Osburn, South African J. M. Sc., 9: 143 (Nov.) 1944; through Trop. Dis. Bull., 42: 455 (June) 1945.

TYROCIDINE

Mice (Swiss)—

Acute Toxicity: LD₁₀₀ in 24 hours was obtained with 25 mgm/kg. in

testing intravenous doses of 1.25 to 30.0 mgm/kg.; and on seventh day with 90 mgm/kg. in intraperitoneal doses of 2.5 to 90 mgm/kg. There was no oral toxicity with dose as large as 1000 mgm/kg. Robinson and Molitor, *J. Pharmacol. & Exper. Therap.*, 74: 75 (Jan.) 1942.

TYROSINASE

Rats—

Experimental Hypertension: Intravenous injection of 180 to 500 units was followed by fall of blood pressure to normal and never rose to previous levels. Normal rats showed slight if any change. Schroeder and Adams, *J. Exper. Med.*, 73: 531; 1941.

Dogs—

Hypertension: Intravenous injection of 5000 to 20,000 units produced similar reaction as in rats, but of shorter duration. Toxic reactions were diarrhea, vomiting, brachycardia. After single injection, it was present in blood for 24 hours, but not a trace was found in human or dog blood after intramuscular or subcutaneous injections. *Ibid.*

Man—

Arterial Hypertension (4 cases): Intramuscular injections of 3 to 8 ml. of heat-inactivated tyrosinase from mushroom caused average fall from 210/150 to 150/90. Local inflammatory response and systemic reactions, such as chills and fever, perspiration, and malaise were observed following injection. Prinzmetal et al., *Proc. Soc. Exper. Biol. & Med.*, 50: 288 (June) 1942.

1-TYROSINE

Rats—

Liver Glycogen was increased by 200 mgm. doses every two hours up to 12 hours in animals previously starved 48 hours. Butts, Sinnhuber, and Dunn, *Proc. Soc. Exper. Biol. & Med.*, 46: 671; 1941.

TYROSINE, FLUORINATED

Rats—

Effect and Toxicity: Basal metabolic rate, 5-iodotyrosine, 15% in rats, were tyro, amphotyrosine. Boyer, Evans, and Phillips, *J. Pharmacol. & Exper. Therap.*, 73: 176; 1941.

TYROTHRICIN

In Vitro—

Yields: 2 gm. per liter or more were obtained after ten to 16 days' incubation of *Bacillus brevis* in 11 mm. layers of asparagus concentrates. Lewis, J. Bact., 50: 236 (Aug.) 1945.

0.0125 mgm. to 0.005 mgm. in 5 ml. were largest amounts permitting culture of *L. acidophilus* to grow. Weinstein and Rammelkamp, Proc. Soc. Exper. Biol. & Med., 48: 147 (Oct.) 1941.

Red Cells: 0.375 mgm. showed some hemolysis in one hour, even in presence of glucose. Tyrocidine and tyrothricin caused greater degree of hemolysis. Weinstein and Rammelkamp, Ibid., 48: 211 (Oct.) 1941.

Mice—

Orally, 0.1–2 mgm. tyrothricin, given daily for three weeks, did not reduce *L. acidophiles* in feces. Weinstein and Rammelkamp, Ibid., 48: 147 (Oct.) 1941.

Mice (Swiss)—

Acute Toxicity: Intravenous doses of 1.2 to 20 mgm/kg. to determine LD₁₀₀; on seventh day with 5 mgm/kg. and within 24 hours with 20 mgm/kg. Intraperitoneal doses of 10 to 90 mgm/kg. gave LD₁₀₀ with 80 mgm/kg. on second day and within 24 hours with 90 mgm/kg. Robinson and Molitor, J. Pharmacol. & Exper. Therap., 74: 75 (Jan.) 1942.

Rabbits—

Experimental Wounds: 1 mgm. powder reduced number of beta-hemolytic streptococci in four out of nine experiments, as compared to one of 16 experiments for 100 mgm. powder sulfathiazole. Neter, Hubbard, and Lamberti, Am. J. Surg., 69: 204 (Aug.) 1945.

Dogs—

Cumulative Toxicity: Daily doses of 2 mgm/kg. caused death after five to six injections. Ibid.

Cows—

Chronic Bovine Mastitis: (Strep. agalactiae) 80 to 160 mgm. instilled 12 to 18 hours brought 82% cures. Schalm, J. Am. Vet. M. A., 100: 323; 1942.

Streptococcus Mastitis Therapy: 50% mineral oil containing 1.5 mgm. per ml. instilled into 130 infected quarters in 49 cows. Average of 2.3 treatments cured 90%. Martin, J. Am. Vet. M. A., 101: 23 (July) 1942.

Man—

Dosage and Use: Drug must be applied locally, not intravenously or by mouth, after diluting with sterile water to form an isotonic solution

in a concentration which yielded 500 micrograms of drug per ml. Reported to be of value in treatment of superficial indolent ulcers, the predominating organisms of which were Gram positive, mastoiditis, empyema, and some other wound infections. Council on Pharm & Chem., J.A.M.A., 124: 985; 1944.

Ophthalmology: 30% solution, four to six times a day, was used in treating pneumococcal conjunctivitis, epidemic kerato-conjunctivitis and dendritic keratitis; 20% solution in blepharitis; irrigation with 30% solution of lacrimal sac three to seven days was effective in low grade dacryocystitis. Heath, J.A.M.A., 124: 152; 1944.

UREA

In Vitro—

Bactericide: Löwenstein-Jensen medium inoculated with 5000 million tubercle organisms incubated for 48 hours at 37° C. in urea dilutions of one-half to one-quarter saturation produced no growth. Brit. M. J., I: 609; 1942.

92.3 gm. urea in 100 ml. distilled water gave a saturated solution, which at pH 6.8 was bactericidal for human, bovine, and avian strains of tubercle bacilli. Cummins, Brit. M. J., I 841, 1945.

Denaturation of Diphtheria Antitoxin: 7.5 molar urea at pH 7.82 destroyed nearly one-half the activity in 24 hours, as measured by neutralizing power of toxin. Wright, J. Exper. Med., 79: 455 (Apr.) 1944.

Man—

Dental Caries: Saturated solution used as dentifrice for two years caused individual reduction of 80 to 100% in caries rate. Stephan and Miller, Proc. Soc. Exper. Biol. & Med., 55 101 (Feb.) 1944.

Diuresis: 60 to 90 gm. daily resulted in satisfactory diuresis in refractory edema. Freedberg and Blumgart, New England J. Med., 227: 874 (Dec.) 1942.

Gonorrhea: 20, 40, or 60 gm. in liquid form were given daily to groups of 50 patients each, respectively, along with sulfonamides. Only slightly better response was shown with urea. It had no significant effect on blood levels of sulfonamides. Urinary output was increased from 823 to 1200 ml. per day. Menville and Ross, J. Urol., 54 211 (Aug.) 1945.

VACCINE VIRUS, YELLOW FEVER

Man—

Dosage: Virus dosages of ten minimal lethal doses (50% mortality probability in mice) gave irregular immunization in man and 100 mini-

mal lethal dose per person could be considered a safe minimum. Bugher and Smith, *Am. J. Hyg.*, 39: 52 (Jan.) 1944.

VACCINE, YELLOW FEVER

Monkeys (Rhesus)—

Yellow Fever: Subcutaneously, 0.5 ml. of 1:10 dilution dehydrated virus (vaccine) nine times over two week period immunized against challenging dose of virulent virus inoculated five days later. Circulating antibodies appeared seven or more days after vaccination. Smithburn and Mahaffy, *Am. J. Trop. Med.*, 25: 217 (May) 1945.

Man—

Immunity: Protective serum antibodies appeared on seventh post-vaccination day in one and tenth day in nine out of ten men. *Ibid.*

Liver Necrosis: Prophylactic injection of vaccine was followed in ten days by severe epigastric pain, vomiting and fever of 103° F.; later, slightly jaundiced, delirious and death 14 days after vaccination. Extensive necrosis of liver was observed at post-mortem examination. Van Langenberg, *Lancet*, 246: 244 (Feb.) 1944.

VANILLIN

Rabbits—

Detoxication: 2.0 gm. was given orally. Excreted in urine: 69% as vanillic acid, 14% as unoxidized vanillin. 44% of vanillic acid was free and 25% conjugated. Sammons and Williams, *Biochem. J.*, 35: 1175; 1941.

VENOM

In Vitro—

Acetylcholine Inhibition: 0.2 to 0.4 mgm. cobra venom inhibited acetyl choline. Ghosh, De, and Sarkar, *J. Indian Chem. Soc.*, 21: 93 (Mar.) 1944.

Pigeons—

Minimal Lethal Dose of dry cobra venom was 0.1 mgm. for pigeon of 320 to 390 gm; that of neurotoxin was 0.0065 mgm. *Ibid.*

Mice and Rats—

Interaction with Thiamine: Resistance to lethal effect of venom was increased by moderate doses of thiamine (four to 10 international units simultaneously with venom, or two to eight international units daily for two to three days before venom injection), decreased by excessive doses of venom (ten international units venom daily for two to three

days before venom injection), or by a diet deficient in thiamine. Thiamine did not antagonize analgesic action of venom. Macht and Spencer, J. Am. Pharm. A. (Scient. Ed.), 31: 146 (May) 1912.

Man—

Angina Pectoris: Injection of ten mouse units (1.0 ml) of cobra venom three times on first day, followed by one injection daily for seven days. Effect maintained by bi-weekly injections of 1 ml. Clinical improvement in seven of 12. Freedberg and Riseman, New England J. Med., 233: 462 (Oct.) 1915.

Arthritis: Lyophilized solution of whole venom of honey bee (*Apis mellifica*) was added to 12.5% magnesium sulfate and 10% glucose. Two doses of 0.05 ml. was given intracutaneously over maximum area of tenderness in a single joint at weekly intervals. Dose increase was 0.1 ml. at each treatment with maximum dose of 1 ml. Cohen et al., Pennsylvania M. J., 45: 957 (June) 1912.

VERATRONE

Man—

Eclampsia: Hypodermically, 0.3 to 0.6 ml. every 15 minutes until pulse rate and blood pressure dropped to normal. In addition, 6 ml. of 50% magnesium sulfate, intramuscularly given immediately, then 1 ml. every six hours, and finally 4 ml. every 12 hours for 48 hours. Greene, Am. J. Obst. & Gynec., 50: 427 (Oct.) 1915.

Prevented by frequent small injections of 0.12 to 0.6 ml. (average 0.2 to 0.3 ml.). Magnesium sulfate acted synergistically in producing vasodilatation. Harkins, Texas State J. Med., 11: 143 (July) 1915.

VINBARBITAL SODIUM

Man—

Pre-anesthetic Dosage: 0.2 gm. rectally for middle aged patients; 30 mgm. with 8 mgm. morphine sulfate and 0.15 mgm. scopolamine was sufficient for patients over 60 years. 0.1 gm. if given alone. For cyclopropane anesthesia, only one half of usual dose was given two hours pre-operatively. Lorhan, Anesthesiology, 5: 370 (July) 1911.

Sedation: Orally, 0.032 to 0.2 gm. (most often 0.1 gm.) either once or three times in the evening or up to four times a day. For profound sedation 0.2 gm. was given every two hours until result was obtained. No serious toxic reaction was observed, effect was gradual, and duration brief. There was no evidence of habituation or tolerance. Hendrix, Am. J. M. Sc., 201: 93 (July) 1912.

VINETHENE

Man—

Dental Anesthesia: Five to 100 ml. (average 30.2 ml.) three to 30 minutes (average 9.3 minutes) required for operation, and two to 25 ml. (average 7 ml.) required for loss of consciousness 0.5 to 7.0 minutes (average 1.37 minutes). Wellman, Kable, and Livingstone, *J. Am. Dent. A.*, 30: 1883 (Dec.) 1943.

VINYL CYANIDE

Laboratory Animals—

Toxicology: 0.33 mgm/liter (153 parts per million) in air was definitely toxic to guinea pigs, rats, and rabbits and much more to monkeys and cats. Caused eye and nose irritation, anorexia, gastrointestinal disturbances and weakness of hind legs. Recovery was rapid. There was no cumulative action. Dogs were most sensitive, showing toxic effects as little as 0.063 mgm/liter. Dudley, Sweeney, and Miller, *J. Indust. Hyg. & Toxicol.*, 24: 255 (Nov.) 1942.

VIRUS, RABIES

Mice—

Immunization: 1 ml. of irradiated tissue culture virus containing 50,000 mouse intracerebral lethal doses was necessary. Webster and Casals, *J. Exper. Med.*, 73: 601; 1941.

VITAMIN A

Rats—

Storage: Feeding on diets containing three, six, and 12 international units per gm. of air-dry food for 28 days showed liver storage that increased with intake level and age as determined by the single-feeding bioassay method. Campbell et al., *J. Nutrition*, 30: 343 (Nov.) 1945.

Requirements: Minimum was eight international units daily or 20 international units per kg 25 international units daily produced optimum growth; 50 international units daily for optimum blood concentration; and 100 international units daily for good liver reserves. Lewis et al., *Federation Proc.*, 1, part II: 121; 1942.

Toxicity: 25,000 to 50,000 international units vitamin A acetate daily given to young rats (69 to 79 gm.) always caused fracture of bones in eight to 20 days. 50,000 international units to pregnant rats caused fatal uterine hemorrhage under internal, and excessive bleeding from minor external injuries occurred. Moore and Wang, *Biochem. J.*, 37: viii (Sept.) 1943.

Guinea Pigs—

Storage: 2 mgm./kg. per day of carotene caused storage of vitamin A in liver, or 0.3 mgm. vitamin A/kg. per day for two or three weeks. 0.6 mgm. vitamin A in liver was lost in 15 to 30 days on vitamin A deficient diet. Bentley and Morgan, *J. Nutrition*, 30: 159 (Sept.) 1945.

Hens—

Carotenoid Metabolism Pigment content of egg yolk was significantly lowered on 15,000 international units/0.5 kg diet and maximum lowering to 25% of basal level with 200,000 international units in diet. No change in yolk vitamin A from basal level of 46.8 international units per gm. occurred below 30,000 level. Vitamin A increased as follows: 30,000 international units, 51.6; 60,000 international units, 62.3; 100,000 international units, 99.3; 200,000 international units, 120.7 (maximum 226 international units). There was similar progressive increases in body fat. basal was 32.3 international units per gm.; with 200,000 international units, 222.6 international units. Vitamin A increased in liver to a maximum in 60,000 international units, and further increases did not augment content in liver. Deuel et al., *J. Nutrition*, 26: 273 (Dec.) 1943.

Turkeys—

Sto
cause
dose
others, both groups were on vitamin A deficient diets. Jukes, *Poultry Sci.*, 21: 357 (July) 1942.

Dogs—

Requirement: 500 international units (weighing 0.1 mgm.) were sufficient to prevent abnormal changes in puppies Mellanby, *Proc. Roy. Soc., London, s. B.*, 132: 28 (Mar.) 1944.

Foxes—

Minimum Requirement: 15 to 25 international units per kg. per day for growing pups. Liver storage resulted when 50 to 100 international units per kilo per day was fed. Smith, *J. Nutrition*, 24: 10; 1942.

Growth of Silver Foxes Experimental ration supplying 0.1 to 0.2 microgram of vitamin per gram of wet feed caused growth of animals to maturity. Coombes, Ott, and Wisnicky, *North Am. Vet.*, 21: 601; 1940 #10; through *Exper. Station Rec.*, 85: 384 (Sept.) 1941.

Pigs—

Requirement: Minimal was about 300 international units of B-carotene or 100 international units of preformed vitamin A daily per 4.5 kg. live weight. Brande et al., *Biochem. J.*, 35: 693 (June) 1941.

Cows—

Acetonemia Therapy: 100,000 to 250,000 units daily for three days. Vitamin therapy should replace chloral hydrate therapy. Patton, Vet. Med., 39: 150 (Apr.) 1944.

Calves—

Relation to Vitamin C: Plasma vitamin A falling below 0.1 microgram per ml. caused level of plasma vitamin C to decrease. Boyer et al., J. Nutrition, 23: 525 (May) 1942.

Requirements: Blood plasma level of ten gammas or more per 100 ml. was adequate vitamin A intake; and seven to eight gammas per 100 ml. was borderline level. Daily intakes of vitamin A which maintained deficient, borderline, and adequate concentration of blood plasma vitamin A were: six, 12, and 18 gammas per kg. body weight, respectively. Daily carotene requirement necessary to maintain adequate plasma vitamin A and prevent deficiency symptoms was 75 gammas per kg. for Holstein yearlings and 125 gammas per kg. for Guernsey yearlings. Blood plasma carotene levels which would maintain adequate blood vitamin A were 50 to 70 gammas per 100 ml. for Holsteins and 110 to 140 gammas, carotene per 100 ml. for Guernseys. Boyer et al., J. Dairy Sci., 25: 433 (May) 1942.

Man—

Absorption: Mean maximum blood level in Evelyn photoelectric units after 7,000 U.S.P. units per kg. were taken orally were: for normal persons, 354; patients with tuberculosis, 160; mild intestinal symptoms, 243; and moderate to severe intestinal symptoms, 127. Breese, Watkins, and McCoord, J.A.M.A., 119: 3; 1942.

Excretion in Urine: Never found in healthy, normal (104 patients) following saturation with 100,000 international units, but appeared in pregnant women and infants. Excreted in urine in kidney disease, liver disease associated with damage of reticulo-endothelial system, infective disease associated with high temperature and neoplasms. Tomaszewski, Edinburgh M. J., 49: 375; 1942; through Internat. Abstr. Surg., 76: 98 (Jan.) 1943.

Human Milk: Average amount of vitamin A in human milk varied from 171 to 331 international units per 100 ml. from an eight day to two months' period in women without vitamin A supplement. Orally, 200,000 international units daily gave maximum level of 2160 international units per 100 ml. during two to ten day period following parturition. Hrubetz, Deuel, and Hanley, J. Nutrition, 29: 245 (Apr.) 1945.

Plasma Concentration was more sensitive than dark adaptation as indicator of vitamin A deficiency. Lower limit was 45 international units per 100 ml. for infants and 67 international units per 100 ml. for children of six to 12 years. Bodansky, Lewis, and Haig, *Science*, 91: 370 (Oct. 17) 1911. 282 micrograms per 100 ml. was found in a patient with renal disease of nephritic or nephrosclerotic origin and 90 micrograms per 100 ml. in controls six hours after administration of 75,000 units of vitamin A. Popper, Steigmann, and Dymiewicz, *Am. J. Clin. Path.*, 15: 272 (July) 1945. Plasma levels were nine to 95 micrograms per 100 ml. (average 32) and carotenoid levels were five to 135 micrograms per 100 ml. (average 59) for hospital patients. Vitamin A level of 9.7 to 85.9 micrograms per 100 ml. and carotenoid levels of 21 to 144 micrograms per 100 ml. were obtained for 55 patients with various skin disorders. Cornbleet, Popper, and Steigmann, *Arch. Dermat. & Syph.*, 49: 103 (Feb.) 1911.

Avitaminosis A Detection Examination of conjunctiva, because conjunctival changes precede dark adaptation. Kruse, *Science*, 95: 623 (June 19) 1912. Patient, seated in dark room, looks directly for three minutes into a light (60 to 100 watts) at eye level about six inches from eye. Patient's head turned to black bulb (7.5 or 10 watts) about 12 inches from eyes. This bulb has a number (half inch long) scratched on with pin. Brighter light turned off and black light turned on. If patient takes five minutes or more to recognize number on black bulb, he lacks vitamin A. 25,000 units vitamin A per day given if it took six minutes, and 5000 units extra per day for each additional minute. Kolb, *J. M. Soc. New Jersey*, 41: 24 (Jan.) 1911.

Color Blindness Treated with 25,000 units daily for three to eight weeks. 50,000 units acted rapidly, but upset digestive tract. Dunlap and Loken, *Science*, 95: 554, 1912. 50,000 units were given daily for four weeks to 13 color blind patients. After four weeks, six were given additional vitamin therapy for four weeks. Blood levels before therapy were 158 international units per 100 ml., 217 after four weeks and 230 after eight weeks of treatment when level was 175 international units per 100 ml. in those who had four week treatment only. There was temporary improvement in color vision in only one. Hamilton, Briggs, and Butler, *Am. J. Physiol.*, 140: 578 (Jan.) 1944.

Dark Adaptation There was no correlation between vitamin A intakes and dark adaptation readings in children. However, after intakes reached 150 international units per kg. there were no cases of subnormal dark adaptation. Oldham, *J. Pediat.*, 20: 740 (June) 1942.

Xerophthalmia, poor night vision, dry skin with acne treated with 5,000 to 25,000 international units per day; retarded growth with 25,000 to 50,000 international units; alopecia with dry skin 25,000 to 100,000 international units; and essential hypertension with 200,000 to 300,000 international units per day. Kolb, J. M. Soc. New Jersey, 41: 24 (Jan.) 1944.

Dermatology: Therapeutic dose was 25,000 to 200,000 U.S.P. units for keratinization of epithelium. Novy, California & West. Med., 56: 144 (Mar.) 1942.

Chronic Arterial Hypertension: 180,000 units for several days lowered blood pressure 30 to 40 mm. Hg. After this 90,000 units was given daily for several months. Govea and Villaverde, Rev. Cubana de Cardiologia, 2: 299 (Sept.-Dec.) 1940; through J.A.M.A., 118: 1418; 1942.

Ichthyosis Therapy: Orally, 60,000 to 100,000 international units for several months and intramuscularly, 100,000 international units in 1 ml. vegetable oil two to three times a week for several months improved congenital ichthyosis. Rapaport, Herman, and Lehman, J. Pediat., 21: 733 (Dec.) 1942.

200,000 U.S.P. units, 0.6 gm. bile salts, and one ampule 1:4000 neostigmine methyl sulfate given daily controlled a case in 51 days. Gordon, Arch. Dermat. & Syph., 52: 178 (Sept.) 1945.

Ichthyosiform Erythroderma: 200,000 units daily produced subjective improvement in a case. Torrey, Arch. Dermat. & Syph., 52: 130 (Aug.) 1945.

Pityriasis Rubra Pilaris: 200,000 units daily controlled. Fox, Arch. Dermat. & Syph., 52: 128 (Aug.) 1945.

Hypervitaminosis A: Painful enlargement of liver, splenomegaly, urobilinuria, hypochromic anemia, hypobilirubinemia, leukopenia and monocytosis, skin paresthesia and cataract occurred in patient who had taken 30 times normal carotene intake (3.5 mgm. per day). Henschen, Schweiz. med. Wchnschr., 71: 331; 1941; through Brit. Chem. Physiol. Abst. A, III: 252 (Mar.) 1942.

240,000 U.S.P. units daily was taken from age of 18 months. Resulted in enlargement of spleen and liver, leukopenia, hypoplastic anemia, advanced skeletal development, clubbing of fingers, increased blood levels of vitamin and lipids, and a thinning and coarsening of hair. Josephs, Am. J. Dis. Child., 67: 33 (Jan.) 1944.

Tuberculosis and Diabetes: 150,000 to 200,000 units vitamin A per day was recommended for pulmonary tuberculosis and diabetes mellitus

accompanied by tuberculosis. Banyar and Cadden, *Dis. of Chest*, 10: 133 (Mar.-Apr.) 1911.

Vincent's Ulceration 12,000 to 252,000 international units of vitamin A produced definite improvement in six and possible improvement in six out of 20. Stammers, *Proc Roy. Soc Med.*, 37: 567 (Aug) 1944.

Excessive Ingestion: Seven million units taken over a period of 40 days resulted in pin point pupils Gerstle, *U. S. Nav. M. Bull.*, 44: 833 (Apr.) 1915.

VITAMIN B

Lactobacillus Casei—

Microbiologic Assay Excellent growth of *L. casei* was obtained when riboflavin, pantothenic acid, nicotinic acid, folic acid, pyridoxine, and biotin were supplied in a suitable basal medium. Omission of any one resulted in absence of growth and acid production. Growth and acid production was proportional to concentration of vitamin under test. Landy and Dicken, *J. Lab. & Clin. Med.*, 27: 1086 (May) 1942.

Rats—

Promin Effect. Orally, 50 mgm. daily for 21 days showed intake of six times as much thiamine, riboflavin and pyridoxine for normal nutrition without side-effects of promin developing. Higgins, *Am. J. M. Sc.*, 207: 239 (Feb.) 1944.

Man—

Experimental Deficiency: Excretion of thiamine fell from 149 to 208 micrograms per day to 7.7 to 11.0 micrograms per day in men on B deficient diet for 23 days. Reactions were apathy, depression, loss of appetite, etc. Treatment consisted of 1 mgm. daily on 23rd day for five days and 5 mgm. per day for next 15 days. Keys et al., *Am. J. Physiol.*, 144: 5 (June) 1945.

Oral Herpes Therapy 5 mgm. riboflavin, 5 mgm. thiamine hydrochloride and 50 mgm. nicotinic acid were given. Recurrent herpes was treated by a maintenance dose of 1 mgm. thiamine hydrochloride daily. Burkett and Hickman, *J. Am. Dent. A.*, 29: 411 (Mar.) 1942.

Requirement: Safe levels for daily intake even in pregnancy and lactation were: thiamine, 3.2 mgm.; nicotinic acid, 40 mgm.; riboflavin, 3.7 mgm.; pantothenic acid, 11 mgm.; biotin, 0.14 mgm.; inositol, 1000 mgm.; pyridoxine, 1.5 mgm.; and folic acid, 1.0 mgm. unit. B vitamins occurred to this extent in a mixed diet of 2,500 calories. Williams, *J.A.M.A.*, 119: 1; 1942.

VITAMIN B.

Bacteria—

Antianemic Factor: One microgram vitamin B₆ conjugate, isolated from yeast, was equivalent to 0.003 to 0.006 microgram vitamin B₆ in stimulating growth of *Lactobacillus casei* and *Streptococcus faecalis*. Pflüger et al., Science, 102: 228 (Aug. 31) 1945.

Man—

Anemia: Initially, 600 micrograms, gradually increased to 1500 micrograms per day for four weeks increased hematocrit readings and plasma globulins. Urinary excretion of B₆ factor was lowest in those with highest plasma globulin content. Sharp, Vonder Heide, and Wolters, J.A.M.A., 124: 734; 1944.

VITAMIN B₆

Chicks—

Requirement: 275 to 300 micrograms of B₆ hydrochloride per 100 gm. of ration was minimum level for optimum growth. Briggs et al., Poultry Sci., 21: 379 (July) 1942.

Man—

Pregnancy: Intramuscularly, 5 mgm. every two to six days for two to six injections relieved nausea and vomiting. Varsas, Bol. Soc. Chilena de obst. y ginec., 8: 404; 1943; through Am. J. Obst. & Gynec., 50: 347 (Sept.) 1945.

VITAMIN B COMPLEX

Mice—

Physiologic Action: 20 gammas/100 gm. of B₂ prevented death in animals given M.L.D. nicotine (0.372 mgm/10 gm.) 20 minutes later. Inoue and Ako, Rika Kenkyu Sho Iho (Bull. Inst. Phys. Chem. Research) 19: 781; 1940; through Far Eastern Sci. Bull., 3: 39 (Sept.) 1943.

Man—

Deficiency: Deficiency simulated senile psychosis. 12 years existent mental and physical symptoms improved within two months after daily doses of 0.6 to 1.05 gm. nicotinic acid given orally; 0.01 to 0.02 gm. riboflavine orally, 0.05 gm. thiamine hydrochloride parenterally, and 15.0 gm. brewer's yeast orally. Meyersburg, New England J. Med., 233: 173 (Aug.) 1945.

Polyneuritis. 100 mgm. B complex subcutaneously and 10 mgm. thiamine orally three times a day for 52 days caused recovery from polyneuritis from carbon tetrachloride absorption through hands. Farrell and Senseman, Rhode Island M. J., 27: 334 (July) 1944.

Diagnostic Test for Beriberi: For incipient or actual beriberi, 10 gm. in aqueous solution was injected intramuscularly daily, for four days and urinary excretion was observed. Normals excreted 50%, and patients with beriberi excreted 20% or less. Ishihara, Kaigun Gunikai Zassi (J. Naval M. A.), 30: 303; 1941; through Far East Sci. Bull., 2: 77 (Sept.) 1942.

Nail Dystrophy: Vertical ridges and fissuring of fingernails partly disappeared with 3 mgm. thiamine hydrochloride, three times a day for six months, and completely disappeared with two vitamin B complex capsules three times a day. Stokes, M. J. Australia, 30: 408 (Nov.) 1943.

Diabetes: Orally, 36 to 45 mgm. thiamine, 21 to 36 mgm. riboflavin; 200 mgm. niacinamide; 3 mgm. pyridoxine; 12 to 27 mgm. calcium pantothenate; 210 mgm. choline; 27 to 150 mgm. inositol; 60 to 280 micrograms *L. casei* factor; and sometimes 225 mgm. ascorbic acid were given daily in divided doses after meals. Parenteral treatment consisted of 20 to 60 mgm. thiamine; 5 to 10 mgm. riboflavin; 50 to 250 mgm. niacinamide; 5 to 10 mgm. pyridoxine; and 5 to 50 mgm. calcium pantothenate, intramuscularly given daily or on alternate days. B complex deficiency appeared to be an etiologic factor in diabetes mellitus. Biskind and Schreier, Exper. Med. Surg., 3: 299 (Nov.) 1945.

Diabetic Neuropathy: Marked improvement resulted with prolonged vitamin B complex therapy in 72 of 100 patients in six to 12 months. One patient received 50 mgm. thiamine hydrochloride per day parenterally and then 25 mgm. with vitamin B complex given orally. Rudy and Epstein, J. Clin. Endocrinol., 5: 92 (Feb.) 1945.

Postpartum Involution: Six to 8 mgm. each of thiamine and riboflavin; 1.5 to 2 mgm. pyridoxine, 90 to 12 mgm. calcium pantothenate; 30 to 40 mgm. niacin; and other B complex factors derived from liver and/or rice and yeast daily accelerated postpartum involution. Biskind and Biskind, West. J. Surg., 52: 266 (June) 1944.

VITAMIN D

Chicks—

Assay: Combined slope in comparative tests of tibia and toe ash in chick assay for vitamin D. Estimate could be made with equal precision and more easily from toe ash than from tibia ash. Bliss, Poultry Sci., 21: 534 (Nov.) 1945.

Mice—

Ultraviolet Radiation: Repeated radiation plus 65 to 800 U.S.P. units

vitamin D per square centimeter each week (total dose 4000 units) did not show hypervitaminosis lesions on autopsy. Blum and Lippincott, J. Natl. Cancer Inst., 2: 623 (June) 1942.

Rats—

Assay: Based on fact that vitamin B promoted retention of radioactive strontium in rachitic rat. Weissberger and Harris, J. Biol. Chém., 144: 287 (June) 1942.

Calcium Absorption: 7200 international units daily failed to influence absorption of calcium from intestines. Patwardhan and Chitre, Indian J. M. Research, 30: 81 (Jan.) 1942.

Dentin Apposition: 2.33 micra per day in 20 female animals given 10,000 U.S.P. units vitamin D as compared to 0.94 micra per day for controls. Ziskind et al., J. Dent. Research, 22: 457 (Dec.) 1943.

Hypervitaminosis D: 13,000 to 29,000 international units daily in form of viosterol for six to 19 days to partially nephrectomized rats led to marked calcium deposition and to renal damage. Oppen, Arch. Path., 31: 569 (May) 1941.

Skeletal Deformities: Rachitogenic diet causing 45% skeletal deformities in offsprings was corrected by addition of 60 U.S.P. units vitamin D to maternal diet. Warkany, Am. J. Dis. Child., 66: 511 (Nov.) 1943.

Wheat Flour: 4.5 gm. wheat flour controlled rachitic signs in rats on rachitogenic diet for ten days. There are 300 international units vitamin D per 100 gm. of wheat germ flour. Lecoq, Bull. soc. chim. biol., 25: 168 (Apr.-June) 1943.

Dogs—

Capillary Permeability: Decreased five to eight days after large doses; e.g., 45,000 to 110,000 international units vitamin D/kg. given in 24 to 48 hours. Silver, Irving, and Reed, J. Lab. & Clin. Med., 29: 48 (Jan.) 1944.

Overdosage: 10,000 international units per kg. per day to a total of 1,500,000 international units presented signs of cachexia, lassitude, anorexia, polyuria, polydipsia, hyperglycemia, and diarrhea five months later. Becks et al., J. Dent. Research, 24: 193 (June-Aug.) 1945.

Man—

Requirement in Children: 300 to 400 U.S.P. units daily produced excellent physical development. 2000 units or more daily caused anorexia and slowed skeletal development. Sterns, J. Lancet, 63: 344 (Nov.) 1943.

Rickets Treated with Massive Doses: 50,000 units at one month of age; 50,000 units at two months of age; and 60,000 units about three months was considered a safe and effective plan. Then 600,000 units to be given every four months. Wolf, J. Pediat., 24: 167 (Feb.) 1944.

Rickets: 600 to 800 units daily protected one-third of infants under six months of age, 2000 units protected all under one year, 3000 units prevented disease in one to two year olds. Mild rickets responded to 1500 units daily in infants of less than one year, 3000 units daily in children one to three years. Severe rickets required 3,250 units daily. Krestin, Arch. Dis. Childhood, 20: 28 (Mar.) 1945; through J.A.M.A., 129: 94; 1945.

Absorption Therapy: Rickets in infants were effectively treated with rubbing twice daily 11,500 units vitamin D in form of irradiated ergosterol. Wagner and Jones, Ohio State M. J., 37: 249 (Mar.) 1941.

Dermatology: 10,000 to 500,000 units daily arrested chronic pemphigus. Novy, California & West. Med., 56: 144 (Mar.) 1942.

Otorhinolaryngology. 65,000 units daily was given for spasm of larynx due to thyroid dysfunction and 100,000 units for spasmodic rhinitis. Bompert and Montero, Prensa méd. argent., 29: 218 (Feb.) 1942; through Quart. Rev. Otorhinolaryngol., 1: 103 (Mar.) 1942.

Parathyroid Tetany Therapy: Doses in six women with permanent and severe tetany varied from 150,000 to 400,000 U.S.P. units daily; duration of treatment was two years or longer in four patients, one and a half and seven months in one patient each. They were on unrestricted diet plus 3 gm. calcium chloride per day. Sevringhaus and St. John, J. Clin. Endocrinol., 3: 635 (Dec.) 1943.

Hypercalcemia: 500,000 to 600,000 international units daily for five years completely healed vitamin D resistant rickets. Increasing attacks of hypercalcemia necessitated reduction to 12,500 units daily. MacLay and May, Proc. Roy. Soc. Med., 38: 565 (Aug.) 1945.

Massive Doses for dental caries prevention. Orally, 600,000 U.S.P. units in form of crystalline D₂ in 1 ml. of oil was given two to three times a year. Brodsky, Schuck, and Vollmer, Am. J. Dis. Child., 62: 1183 (Dec.) 1941.

Fatalities: Five deaths have been reported so far. Massive single doses did no harm but continual use of large doses produced toxicity. Toxic dose is difficult to define. 20,000 international units per kg. was stated to be toxic, although doses as low as 1000 international units per kg. have produced toxic effects and even 400 international units per kg. caused death in a child. Question, Brit. M. J., 1: 173 (Feb.) 1945.

Toxicity: 150,000 to 200,000 units daily for six years taken for arthritis by one patient caused deafness, renal insufficiency, anemia and calcium deposit in tissues. Danowski, Winkler, and Peters, Ann. Int. Med., 23: 22

(July) 1945. Orally, 150,000 to 450,000 international units per day was given intermittently for five years to a child with vitamin D resistant rickets. Non-rachitic bone disturbances occurred with 450,000 units daily and toxic reactions suddenly developed after 15 months of treatment with 40,000 units per day. Dosage was reduced to 100,000 units, then to 50,000 units when severe dehydration and vomiting developed. Mackay and May, Proc. Roy. Soc. Med., 38: 563 (Aug.) 1945.

VITAMIN D₂

Dogs—

Experimental Hypoparathyroidism: A single dose of 2 mgm/kg. of either D₂ or D₃ produced a rise of serum calcium from seven to 8 mgm.% to 11 to 12 mgm.% for 25 to 35 days in animals on a diet of medium calcium and phosphorus content. McChesney and Giacomino, J. Clin. Investigation, 24: 680 (Sept.) 1945.

Massive Dose Effect: 900,000 international units produced pathologic calcification of hard and soft tissues of jaws, lungs and kidneys. Morgan et al., J. Dent. Research, 24: 199 (June-Aug.) 1945.

Man—

Rickets in Infants: Orally, 50,000 international units daily for ten days or intramuscularly 200,000 units every other day up to a total of 600,000 units produced immediate and rapid results. Lovell, Rev. Soc. pediat. de Rosario, 7: 19 (Apr.) 1942; through J.A.M.A., 120: 1438; 1942.

Rickets in Children: Single dose of 15 mgm. (600,000 international units) healed active rickets in 38 infants and 13 children, one to two years old. Krestin, Lancet, 248: 781; 1945.

VITAMIN E

(See Tocopherol, Alpha p. 338)

Bitterlings (male)—

Assay: 5 mgm. alpha tocopherol acetate added to 750 ml. water produced within a few hours nuptial colors in male bitterling. Duyvené, Klin. Wchnschr., 20: 1171; 1941; through Biochem. Ztschr., 309: 297; 1941; also Die Chemie, 55: 66 (Feb.) 1942.

Man—

Habitual Abortion: Ten mgm. progesterone daily for three days, then less for additional two days. Optimal dose of vitamin E was 30 mgm. Combination of both was ideal for therapy. Bach, Arch. f. Gynak., 172: 97; 1941; through Ztschr. f. Vitaminforsch., 12: 182; 1942.

Primary Fibrositis: Orally, 120 to 240 mgm. daily and intramuscularly 334 mgm. total tocopherols at weekly intervals for three weeks showed good results. Also 200 mgm. synthetic alpha tocopherol in corn oil weekly for two to four months led to relief Steinberg, J. Bone & Joint Surg, 24 411 (Apr.) 1942.

VITAMIN K

Chicks—

Assay: Day old chicks fed vitamin K deficient diet until clotting time was 15 minutes, then divided into one group for control, one group for assay, and one group for varying doses of standard reference 2-methyl-1,4-naphthoquinone. After four days, prothrombin time determined and compared. J.A.O A.C., 24 84; 1941.

Dogs—

Hemorrhagic Diathesis: Orally, 0.08 gm. daily corrected prothrombin deficiency after biliary fistula operation. Therefore compound was absorbed from intestine in absence of bile. Thaddea and Frost, Ztschr, f. Vitaminforsch., 12 134; 1942.

Man—

Chronic Urticaria: 6 mgm. synthetic vitamin K relieved 62% of patients Where prothrombin time was prolonged, 78% were relieved; where it was normal, 32.5%. Black, J. Allergy, 16 83 (Mar.) 1945.

Dicoumarol Antagonist Single intravenous dose of 0.5 to 1.0 gm. vitamin K oxide inhibited anti-coagulant action of dicoumarol in oral dose of 0.8 gm. initially, and 0.2 gm. daily for three to eight days which prolonged more than 15 minutes of coagulation time. Coagulation time returned to normal in ten hours Davidson, Freed, and MacDonald, J. Clin. Investigation, 33 935 (Nov.) 1944.

Hemorrhage. Intravenously, 60 mgm or more controlled hemorrhage in a few hours Segard, Virginia M. Monthly, 72 378 (Sept.) 1945

Hemorrhagic Disease of the newborn was treated with an average initial dose of one to 3 mgm intravenously, followed by 3 mgm. maintenance dose. Karabin, Illinois M J., 81 56 (Jan.) 1942.

Hypoprothrombinemia One to 3 mgm orally or intravenously maintained normal condition. For immediate response, 6 mgm. was given as initial dose. Ibid

Orally, 5 mgm. at first labor pain was practical in most cases in preventing hypoprothrombinemia in newborn For treatment of existing condition of hypoprothrombinemia, 2 mgm at 12 hour intervals, was given parenterally until value returned to normal or bleeding stopped. Waddell, J. Pediat., 20. 656 (May) 1912.

Menorrhagia and Metrorrhagia: Intramuscularly, 10 mgm. on each of first two days, followed by daily oral administration produced 16 successes out of 17 cases. Dietz, München. med. Wchnschr., 88: 1009; 1941; through J.A.M.A., 119: 1060; 1942.

Prophylaxis in Obstetrics: 2 mgm. daily for four days prior to onset of labor reduced infant mortality to 1.9%; and 3.9 in controls. Hellman and Shettles, South. M. J. 35: 289 (Mar.) 1942.

Prothrombin in Newborn: Intramuscularly, 1 mgm. synthetic preparation (4-amino 2-methyl-1-naphthol hydrochloride) given within four hours after birth maintained normal prothrombin times throughout first six days of life. Richdorf, J. Lancet, 62: 155 (May) 1942.

Prothrombin Time: Intravenously, 64 mgm. menadione bisulfite reduced prothrombin time to safe values within 18 hours from more than 60 seconds following dicoumarin. Cromer and Barker, Proc. Staff Meet., Mayo Clin., 19: 217 (May) 1944.

Requirement in newborn infant was one microgram. Sells, Walker, and Owen, Proc. Soc. Exper. Biol. & Med., 47: 441 (June) 1941.

VITAMIN K₅

(2-methyl-4 aminonaphthol-1 hydrochloride)

Rats—

Toxicity: Oral lethal dose was 0.7 gm/kg. Veldstra and Wiardi, Rec. trav. chim., 62: 75 (Jan.) 1943.

Man—

Effect: Excellent clinical results were obtained with 2 to 3 mgm. parenterally and 5 mgm. orally. Ibid.

VITAMIN K₆

(2-methyl-1,4-diaminonaphthalene-di-hydrochloride)

Rats (albino)—

Toxicity: Oral lethal dose was 0.7 gm/kg. Veldstra and Wiardi, Rec. trav. chim., 62: 75 (Jan.) 1943.

Man—

Prothrombin Time: Restored to normal within 36 hours with oral 5 mgm. dose given to eight premature children. Ibid.

VITAMIN P

Man—

Capillary Fragility. 100 mgm. daily cured abnormal capillary fragility in 12 allergic children. Rapaport and Klein, J. Pediat., 18: 321 (Mar.) 1941.

VITAMIN PP

Man—

Infant Eczema: Intramuscularly, 100 mgm. daily for seven to ten days, then every other day for ten days and two to three tablets containing 200 mgm., by mouth, on days between injections days caused symptoms to disappear in 15 to 20 days. Murano, *Riforma med.*, #25, June 21, 1941; through *Ugesk. f. laeger*, 103: 1346 (Oct.) 1941.

Liver Levels: 15 mgm/100 gm. fresh liver tissue was about normal content. Gounelle, Raoul, and Marche, *Compt rend Soc. de biol.*, 139: 30 (Jan.) 1945.

Requirement: Ingestion of 12 to 16 mgm. gave a blood level of six to 6.5 mgm. Daily ingestion of 15 to 20 mgm. was recommended Gounelle, Vallette, and Raoul, *Compt. rend Soc. de biol*, 139: 16 (Jan.) 1945.

VITAMINS

Man—

Cold Therapy: Cod liver oil concentrate containing 150,000 units vitamin A and 15,000 units D divided in three equal doses for first 24 hours; 50,000 units A and 15,000 units D on second day, and if symptoms persisted, 100,000 units A and 10,000 units D on third day controlled 30.3% of 112 patients. Crampton, *New York State J. Med.*, 44: 162 (Jan.) 1944.

Idiopathic Ulcerative Colitis was treated with five to 10 mgm. thiamine hydrochloride, 25 mgm. nicotinic acid, 5 mgm. riboflavin, 25 mgm. pantothenic acid, 25 mgm. pyridoxine, 50 to 100 mgm. ascorbic acid, 6000 international units vitamin A, 600 international units vitamin D and 1 to 2 mgm. vitamin K. Elsom, *Pennsylvania M. J.*, 45: 697 (Apr.) 1942.

Infantile Pellagra: Vitamin therapy intensified accumulation of fat in liver. Two had received 100 mgm. nicotinic acid, 10 mgm. thiamine, and 50 mgm. vitamin C twice a day by injection plus brewer's yeast and halibut liver oil. Gillman and Gillman, *J A.M.A.*, 129: 12; 1945.

Neurologic Disorders Orally, 75 mgm. vitamin E, 6 mgm. thiamine hydrochloride, 3 mgm. riboflavin, 15 mgm. pyridoxine hydrochloride, 30 mgm. niacinamide, and 3 mgm. calcium pantothenate per day for nine and a half weeks Intrathecally, 25 mgm. thiamine hydrochloride in saline once weekly, starting two weeks after oral therapy was begun, increasing each successive dose by 25 mgm. until 100 mgm. was reached and continued for eight injections. Heilbrunn and Hollenberg, *J. Nerv. & Ment. Dis.*, 102: 379 (Oct.) 1945.

Surgical Convalescence 10 gm. vitamin C injected daily and other

injections containing thiamine, riboflavin, and niacin, and also parenteral injection of glucose containing amigen were given to 79 patients with abdominal operations. Oral feeding was resumed as soon as food could be retained. Elman and Akin, *Ann. Surg.*, 122: 716 (Oct.) 1945.

Surgical Requirement: High protein diet plus vitamin concentrates were given two to three weeks prior to operation, consisting of 1 gm. vitamin C, 50 mgm. thiamine, 10 mgm. riboflavin, 100 mgm. nicotinic acid and 2 mgm. vitamin K immediately before and for several days after all operations. Starr, *Intern. Obst. Surg.*, 74: 309; 1942.

XYLOL

Man—

Lymphopathia Venereum was treated with 3 ml. daily with milk as vehicle, gradually increased to 6 ml. daily given in divided doses. Herrera, *Bol. Ofic. san Panamericana*, 20: 1005 (Oct.) 1941; through *Digest of Treatment*, 5: 880 (May) 1942.

YEAST

Pigs—

Nutrition: 114 gm., irradiated dry yeast added to 910 kg. of full-ration feed or 227 gm. per 910 kg. home-grown feed insured adequate vitamin D. Vitamin D-Digest, 5: 35 (Nov.) 1943.

Man—

Precancerous Mouth Lesions were treated with daily administration of 45 gm. granular yeast and liver extract. Martin and Koop, *Am. J. Surg.*, 57: 195 (Aug.) 1942.

Tobacco-Alcohol Amblyopia: Treatment consisted of high vitamin B, well balanced diet, supplemented with 30 ml. brewer's yeast five times daily, 15 ml. autolyzed brewer's yeast extract, three times a day, 60 ml. wheat germ, three times a day, 5 ml. liver extract given intramuscularly several times weekly and 30 ml. cod liver oil, daily. Vision was improved or restored to normal in 25 patients. Carroll, *Am. J. Ophth.*, 27: 713 & 847; 1944.

YOHIMBINE

Rats—

Effect: Concentrations under 1:1000 in drinking water, given over a period of three months, were non-toxic. Adrenolysis: two to 7 mgm. of hydrochloride per kg. or ethyl yohimbine hydrochloride caused salivation and vasomotor reversal. Sympatholysis: salivary reactions with 4

mgm. yohimbine per kg. to 6 mgm. ethyl yohimbine per kg., nictitating membrane reactions with 15 mgm. ethyl yohimbine per kg. to 28 mgm. yohimbine per kg.; mydriatic action with 15 mgm. plus ethyl yohimbine per kg. and 28 mgm. plus yohimbine per kg. Yonkman, J. Lab & Clin. Med., 29: 1222 (Dec.) 1944

Rabbits—

Hyperglycemia: Intravenously, 2 mgm of yohimbine hydrochloride per kg. caused marked hyperglycemia after 30 minutes, followed by marked hypoglycemia. Latter effect was not observed after subcutaneous injection. Katagi, Okayama Igakkai Zasshi, 50 401, 1941; through Far East Sci. Bull., 2: 69 (Sept.) 1942.

ZEPHIRAN

(Mixture of alkyl dimethyl benzyl ammonium chlorides)

Rabbits—

Eye Irritation: Irrigation of anterior chamber with 0.025 to 0.05% solution caused swollen, gray corneal epithelium, marked engorgement of iris vessels, edema of iris stroma, and profuse outpouring of fibrin into chamber; secondary glaucoma or degeneration followed and cornea was usually permanently impaired. Swan, Am. J. Ophth., 27: 1118 (Oct.) 1944.

Local Use: 0.1% in eyes caused conjunctival and corneal changes. 0.03% four times a day retarded epithelial regeneration Leopold, Arch. Ophth., 31: 99 (Aug) 1915.

Man—

Arterial Embolism: 1:1000 solution was used to cleanse affected part in six cases of arterial embolism and gangrene Gross, Am. J. Dis. Child., 70: 61 (Aug.) 1915.

Chronic Infected Ear. Cotton pledget moistened with 1:1000 aqueous solution was placed in middle ear against round window niche. Packs changed every two weeks. Improvement in every one of eight patients. Hughson, Diseases of Eye, Ear, Nose & Throat, 2 258 (Sept.) 1912.

Dental Caries: 1:1000 solution used as dentifrice for two years reduced caries rate to 56-90% as compared to 18 months' period observation. Stephan and Miller, Proc. Soc. Exper. Biol. & Med., 55: 101 (Feb.) 1944.

Ocular Tissues Single instillation of 0.5 ml. of 0.1% solution into conjunctival sac caused hyperemia and edema of conjunctiva and profuse lacrimation. 0.03 to 0.01% solutions three to four times daily for two to eight weeks caused cumulative effect. Returned to normal in 12 hours. Swan, Am. J. Ophth., 27: 1118 (Oct.) 1944.

ZINC

Man—

Excretion: Daily urinary zinc excretion was 0.3 mgm. for normal persons, 2.3 to 3.0 mgm. in patients with albuminuria. McCance and Widdison, *Biochem. J.*, 36: 692 (Sept.) 1942.

ZINC CHLORIDE

Man—

Deaths: Inhalation of fumes of 75 gm. per 8.5 liters caused ten deaths. Reactions were: acute inflammation of respiratory tract, red and running eyes, dyspnea, retrosternal and epigastric pain, stridor, and mental distress. Pulse and respiratory rates increased, and many coughed with copious expectoration. Evans, *Lancet*, 249: 368 (Sept.) 1945.

ZINC PEROXIDE

Man—

Dermatology: 10% in vanishing cream healed ringworm in two weeks. 45% zinc peroxide and 55% zinc oxide in vanishing cream base was used twice daily for dermatophytosis. Feldman, *Arch. Dermat. & Syph.*, 44: 674; 1941.

Mouth Infections: Powder applied to tissues with cotton. Patient's saliva dissolved drug with liberation of oxygen. Used especially for Vincent's stomatitis. Mallett and Guralnick, *J. Am. Dent. A.*, 29: 384 (Mar.) 1942.

Swollen Prepuce: Over 400 cases relieved by powder forcefully blown about glans penis and under foreskin by means of an insufflator. Treatment repeated in two to three days, if necessary. Allison, *J.A.M.A.*, 124: 774; 1944.

